“STUDY OF WAYNE’S DIAGNOSTIC CRITERIA IN HYPERTHYROIDISM”

DISSERTION SUBMITTED FOR

M.S. DEGREE EXAMINATION

BRANCH I GENERAL SURGERY

OF

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI

APRIL-2014

CERTIFICATE

This is to certificate that the dissertation titled**,"STUDY OF WAYNE"S DIAGNOSTIC CRITERIA IN HYPERTHYROIDISM"** is the bona fide original work of **DR.SHALIKH MOIDU** in partial fulfilment of the requirements for **M.S.(General Surgery)** Examination of the Tamilnadu DR.M.G.R. Medical University to be held in April 2014.The period of study was from september 2012 to september 2013.

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DECLARATION

I, **DR.SHALIKH MOIDU**, solemnly declare that dissertion titled "**STUDY OF WAYNE'S DIAGNOSTIC CRITERIA IN HYPERTHYROIDISM**" is a bonofide work done by me at Tirunelveli Medical College Hospital, Tirunelveli during the period of september 2012 to september 2013, under the guidance and supervision of **PROF.DR.S.SOUNDARARAJAN M.S.,**Professor and HOD of General Surgery.

This is submitted to the University of Tamil Nadu, Dr. MGR medical university in partial fulfilment of the rules and regulations for the M.S. Degree Examination in General Surgery.

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Dr. Shalikh Moidu

ABBREVIATIONS

T3 – triidothyronine

T4 – thyroxine

THS- thyroid stimulating hormone

M1- monoidothyronine

M2 – diidothyronine

Solitary – solitary nodule goitre

Diffuse- diffuse goitre

Nil- no clinically evident swelling

MNG- multinodular goitre

SVC- Superior Vena-Cava

NHANES- National Health and Nutrition Examination Survey

Y- Hyperthyroid state

N- Not hyperthyroid state

CONTENTS

INTRODUCTION

Thyroid gland is very important for metabolism of the body, its function is very important from in utero to maturation. . Fluctuation in levels of thyroid hormone from normal have far reaching effects on body's homeostatic mechanism.

The burden of thyroid related disease in the general population is vast. Thyroid related diseases are the most common among all endocrine diseases in India.

In many studies conducted abroad ,half the people in a population has microscopic nodules, less than 15% have thyroid swellings, less than 3.5% are subclinically having occult papillary carcinoma, 10% have aberrant TSH levels and 5% have clinically significant hypothyroidism or hyperthyroidism.

Inspite of the successful coverage of National iodine deficiency diseases control programme (NIDDCP) in India, iodine deficiency is still prevalent in many parts throughout India.

A retrospective cohort study of 325 cases of hyperthyroidism undergone surgery showed that, in more than 180 patients where Graves' disease was the primary etiology followed by more than 100 cases of toxic multinodular goitre and more than 30 cases of (35) functioning nodules.

As a conclusion to introduction, the spectrum of thyroid diseases is very wide and hypothyroid state is out of scope of wayne's index. So, focusing on current problem in India, gives a clear need of Targeted Screening for thyroid diseases in high risk polulation of all age groups is essential. So far biochemical analysis is confirmative of thyroid state quantitavely. Other investigative modalities like FNAC, Scintiliography, Radio-Iodine uptake study, Ultra Sound Scan, Auto-Antibody study are available for confirmation of diagnosis at higher centres. Since, Indian setup of medical services offers certain investigative modalities at certain level of health system it is not possible for primary level of health setup to facilitate diagnosis. Conclusively, Wayne's Index will be useful to apparently quantify clinically the thyroid state of patient and referring the selective to higher centres.

This study aims to find the sensitivity of Waynes's index in correlation with biochemical analysis in our clinical setup and thereby promoting the hypothesis that wayne's index quantification at primary level for screening and referral.

AIMS OF STUDY

1. To quantitavely analyse the accuracy of wayne's clinical criteria in correlation of biochemical investigation.

2. To ascertain the commonest presenting signs and symptoms of hyperthyroidism in contest of the study.

REVIEW OF LITERATURE

HISTORY

Important milestones regarding thyroid and and its disorders, approach is chronologically mentioned below

2780-2280BC – archaeologically, statues in Egypt shows signs of GRAVES'S Disease vaguely.

1600BC- Ancient Chinese healers used burned seaweeds and sponges to treat goitre, found by ancient papyrus.

69-30BC - Idol of Cleopatra in Egypt, once stated to be the most beautiful women in Egypt was found to be with goitre.

130-200AD – Galen coined the term "thyroid" as resembling Shield in Greek language.

1050AD – Abul Abbas, also known as albucasis, described surgical approach to thyroid in written proof.

1563AD – Eustachius – described isthmus as connection between two lobe and named it as well.

1656AD- Wharton – in his book *adenographia,* correctly used term Thyroid but incorrectly described the gland as a gland which lubricate larynx.

1811 AD-papers regarding thyroid cancer published

1825AD – Parry, gave account related to exopthalmic goitre.

1835AD – Graves, as a research paper described the action of overactive thyroid and effects by its hyper activity.

1871 AD- Cretinism, as an effect of thyroid hypo-activity was explained

1874 AD- first research paper regarding myxedema was published publicly.

1881AD- Billroth – Reported an detailed account on 48 thyroidectomies performed since 1877AD, in which only four died. First he was the one to use artery forceps to prevent and stop hemorrhage of surgical site. Noted the presence of post-surgical tetany in many of his patients.

1883AD – Kocher- Discovered method of ligating the thyroid arteries outside the capsule and the gland with an aneurysm needle, and ligating as close to the carotid artery as possible. Used a transverse collar incision now bearing his name. Noted the presence of "cachexia stermipriva" or postoperative myxedema in his total thyroidectomy patients.

1891AD-Thyroid extract therapy practised for the first time for myxedema

1907AD- C. Mayo- first used the term Hyperthyroidism.in 1912 he Operated more than 270 cases of goitre without much morbidity. Recommended to divide the strap muscles for adequate field of surgery (visualization of recurrent laryngeal nerve) & for preservation of the parathyroids to decrease the risk of tetany.

1912 AD-first description regarding Hashimoto's disease

1936AD- Sub acute thyroiditis explained

1946 AD- Structure of thyroxine (T4) elucidated

1952 AD- structure of tri iodo thyronine (t3) elucidated

1956 AD- Earliest evidence of thyroid auto antibodies in Grave's disease

1957 AD-Presence of auto antibodies in Hashimoto's disease was first detected.

1959 AD-Diagnosis of Medullary carcinoma thyroid as a distinct entity was made.

1976 AD-Reports of postpartum thyroididtis with hypothyroidism or

Thyrotoxicosis.

E J wayne a physician who applied statistical methods for the diagnosis of hyperthyroidism half a century back in the year of 1954AD. After the advent of biochemical methods of diagnosis, this criteria got less widely used.

ANATOMY

Thyroid apparatus consists of thyroid gland proper, all variable number of parathyroid glandules, and in some cases portions of thyroid tissue otherwise known as accessory thyroid gland, lying anywhere in the region between base of tongue and aorta.

It is uncertain that the pars intermedia of the pituitary gland may have to be added as the third constituent of thyroid apparatus, since, according to Swale Vincent, it appears to act as substitution of thyroid in case of removal and atrophy of the gland.

The Thyroid Gland consists of two somewhat pear-shaped or shield shaped lateral lobes of reddish-brown colour joined together by an isthmus or median lobe. The lateral lobes are lateralised on either side and in front of the larynx and upper three or four rings of the trachea. Their upper conical poles extend to the middle of the thyroid cartilage, their lower thick and rounded poles reach almost to the line of t he sternum and in some cases retrosternal also. The posterior edge of the left lobe extends back to the oesophagus.

The isthmus is absent in 15 to 20 per cent, of cases; as a rule it is represented by a narrow band lying over the third and fourth tracheal rings, where

it can be readily felt. It is in the isthmus that degenerative and fibrotic changes are liable to begin; consequently failure to detect it clinically may indicate commencing fibrosis. A projection the processus pyramidalis extends upwards from the isthmus or either of the lateral lobes and be attached to the thyroid bone by a fibro-muscular band. The organ follows the larynx in deglutition, in other words moves with deglutition, a fact of importance in its clinical examination.

Thyroid comprises of a capsule which is connective in nature and to the septa in contuinity with it and that encloses stroma of the gland. This comprises the true capsule of the gland.

Pretracheal fascia is a fascial layer outside the above mentioned capsule called false capsule. It is also known as surgical capsule or peri-thyroid capsule. It is considerably reduced posteriorly, helps in increase of gland in the posterior aspect. The ligaments of Berry is thickening of this fascia .

The gland varies considerably in size and weight, its variations to some extent being dependent upon the age, sex, place of residence and state of general nutrition of the individual. It is relatively larger in infants than in adults, forming about 1/800th part of the body weight in the former and 1/1800th part in the latter. In the adult its average weight is 30-50 gm in inland tracts and hilly districts, 20-30 gm at the sea coast. It is roughly one-third heavier in females than in males.

In estimating the increase in size of the thyroid by measurement of the circumference of the neck, it is well to be aware of the fact that in the absence of other factors an increase of ¾ to 1 inch will represent a doubling of its volume, a further increase of 1/2 to 1 inch a tripling, and a still further increase of 1/2 to 3/4 inch a 4 times increase of volume. These values are about true to normal circumference of neck of approximately 15 inches.

SURFACE MARKING

Arch of cricoid as base, then two parallel lines drawn at 1.2cm and 2.5cm downwards from arch of cricoids will mark the isthmus of thyroid.

Upper lobe is pointed and lies at the level of about half of thyroid cartilage, then the lower lobe is extending up to the clavicle. The lateral border roughly overlapped the medial boarder of sternoclidomastoid muscle.

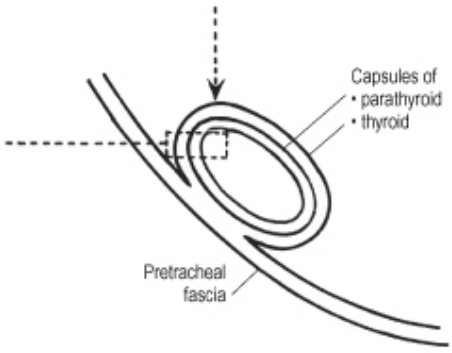
EXTEND

It extends from C5 to T1 vertebra, covering the upper part of trachea. From middle part of thyroid cartilage to fifth tracheal ring. The isthmus extends from second to fourth cricoids ring.

CAPSULE

True capsule is formed by condensation of peripheral connective tissue. It is highly vascular that is why during surgery the gland is removed along with its true capsule.

False capsule is formed from deep cervical fascia. Posterior it is very thin but one condensation called as ligament of berry is present at the posterior surface, this is the reason for it moves with deglutition.



RELATION

Lateral/Superficial Surface: covered by sterno-hyoid, sterno-thyroid, superior belly of omohyoid and anterior boarder of sternocliedomastoid.

Medial Surface : trachea, oesophagus, inferior constrictor muscle, crocothyroid muscle, recurrent larylgeal muscle and external laryngeal nerve.

Posterior surface: over laps carotid sheath therby overlapping internal carotid artery.

Anterior boarder: related to anterior branch of superior thyroid artery.

Posterior boarder : is related to inferior thyroid artery, anastomosis between superior thyroid and inferior thyroid artery, parathyroid gland and left thoracic duct.

Isthmus : connection between two lobes. Sometimes remnant of thyroglossal duct, pyramidal lobe attaches to it.

Anterior surface: covered by right and left sternothyroid and sternohyoid muscle. Fascia and skin

Posterior surface is related to second to third tracheal ring, or it may vary.

Upper border: related to anastomosis between right and left superior thyroid artery.

Lower border: escape point of inferior thyroid vein.

BLOOD SUPPLY

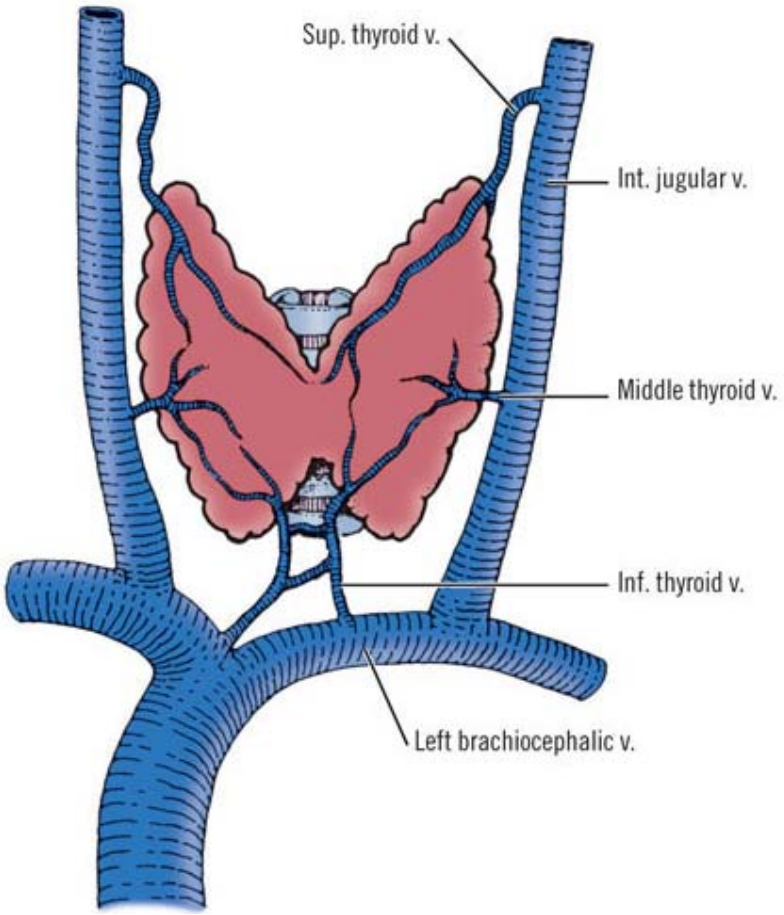
The thyroid is one of the most vascular organs of the body. It is estimated that in proportion to its size it receives more than five times as much blood as the

kidneys, while nearly as much blood passes through its arteries as through the internal carotid and vertebral to the brain. Vasomotor dilatation, therefore, is capable of giving rise to rapid swelling of the gland. The superior and inferior thyroidal arteries form a rich anastomosis on its surface, their smaller branches penetrating with the connective tissue framework between its lobes and lobules. Here they divide and re-divide until each individual follicle is surrounded by a close network of sinus-like capillaries with which the vesicular epithelium is in perfect contact.

Blood supply to thyroid is mainly two pair of arteries. A third vessel sometimes is present and gives supply to lower aspect or pole of either lobe. The superior thyroid artery comes as the foremost branch of ECA (External Carotid artery). It runs below the inferior constrictor and final destination is zenith of lateral aspect or lobe, bifurcates to larger anterior branch and smaller significant posterior branch. Pyramidal lobe may be supplied by a branch from the left side. The vessel from below, inferior thyroid artery is usually bigger in size and vary in anatomy, may be absent or can be double on 1 side in lss than 10 percent of individuals. Its origin is from thyrocervical trunk and passes inferiorly before forming a loop down, and further medial course behind carotid sheath to reach posteriorly and lateral aspect of gland between mid and lower one third of gland.

Abundant accessory vessels spring out from trachea and oesophagus, most significant is thyroidea ima which is also known as Neubauer's vessel or artery, which goes up trachea anteriorly to isthmus or lower part of thyroid. Origin is from brachiocephalic artery or great aorta. Thyroidea ima appears to be an important source of blood supply, if the inferior thyroid artery is absent

Veins:-

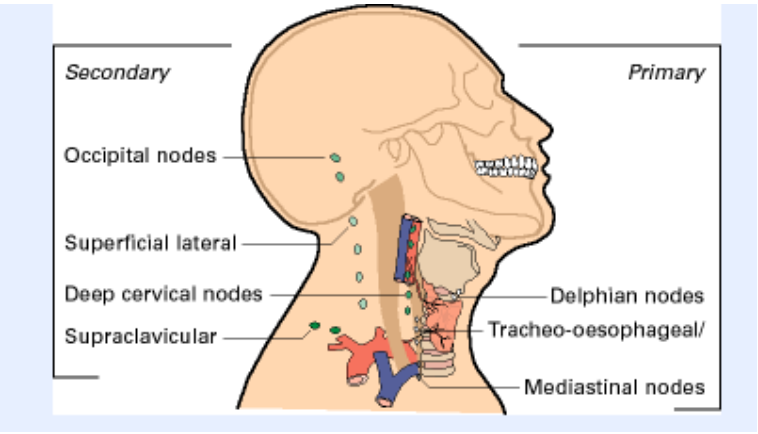


The 3 veins which are named are also same in number like arteries, there is a lot of variabilities in anatomy among these veins. Internal

jugular vein accepts drainage of superior thyroid vein which is a confluence of vessels from the superior pole. Internal jugular vein also accepts the drainage of middle thyroid vein which lies above inferior thyroid artery. From the inferior pole of the lateral part or lobe and isthmus, descend the inferior throid vein, which confluences to the internal jugular vein or joins the brachioocephalic vein which is situated in the superior mediastinum.

LYMPH DRAINAGE

Lymph system is a free flowing system. Lymph spaces lie outside the perivesicular capillaries. These peri-alveolar spaces join with interlobular vessels forming large trunks which anastomose into plexuses lying beneath the capsule of the organ. From these plexuses two main trunks convey the secretion-containing lymph to the circulation by way of the superior and inferior deep cervical glands.



Lymph node drainage from upper area is drained by Delphian nodes sideways or laterally by trachea oesophageal nodes, below to nodes in mediastinum. A specific dye infused to the system shows most of the nodes of the gland diverted to thoracic duct and cervical group and posterior group in the posterior triangle may be bypassed but the paths can be used up secondarily. It is significant in thyroid cancer where lymph can drain outside main areas, may be even to opposite side.

The Lymph drainage of the parathyroid glandules is equally free and joins the lymph system of the thyroid with the secretion from which organ it is intermingled.

NERVE SUPPLY

The thyroid apparatus receives its nerve supply through the superior and inferior laryngeal nerves, from the vagus and from the superior cervical ganglion of the sympathetic. Fibres are distributed to the muscle cells of the vessels and to the secreting epithelium. Its secretory fibres reach the cells from the cervical sympathetic so that the secretion of the gland is directly under the control of sympathetic impulses (Cannon). Cannon states that as the result of experimental stimulation the secretion issues as promptly as in 5 to 7 seconds.

The same observer has shown that when the phrenic nerve is joined to the peripheral portion of the cervical sympathetic in the cat, and the thyroid is thus continuously stimulated as the animal breathes, this operation results in

tachycardia, increased excitability, loose motions, exophthalmos on the operated side, great increase in the metabolism, and in some cases an increase in size of the adrenals.

In thyroid surgery, following nerves, superior laryngeal nerve which the thyrohyoid membrane and recurrent laryngeal nerve which supplies the laryngeal muscles are of utmost significance so it is discussed in detail.

Recurrent Laryngeal Nerves (Inferior Laryngeal):-

Vagus gives the branch, right recurrent laryngeal nerve which it circumvents the right subclavian artery anterior to it. On the right side, nerve circumvents the main vessel, subclavian artery from back to front aspect, it passes across common carotid upward the trachea oesophageal groove. It goes behind thyroid's right lobe and enters laryngeal complex and thyroid cartilage's inferior cornu.

Vagus gives another branch from left side, left recurrent laryngeal nerve. It goes across the aortic arch, origin is just a few millimetre of the origin of arch of aorta, looping under aorta and ligamentum arteriosum and goes upward as right nerve. Right and left nerves goes across inferior thyroid arteries in lower portion of the middle one third of the gland

VARIATIONS:

Many variable courses are noted in anatomy. These variations increase the possibility of surgical morbidity by causing nerve injury

Katz and Nemiroff visualized 1,117 recurrent laryngeal nerves. They reported that 747 (63%) bifurcated or trifurcated more than 0.5 cm from the cricoid cartilage. Bilateral nerve bifurcation was observed in 170 patients.

In an earlier version of this research, these authors wisely concluded that "extralaryngeal branches of the recurrent laryngeal nerve are not an anatomic rarity.

Therefore, thyroid surgery must include identification and preservation of the recurrent laryngeal nerve and all of its divisions."

Right recurrent nerve in less than one percent of cases, takes an abnormal course and goes medially from its beginning to laryngeal complex without forming a loop below subclavian artery.

In this scenario, on right side the subclavian artery originates differently from descending aorta and goes behind oesophagus. This variation is benign and surgeons may be ignorant of this before surgery, rarely a known recurrent left

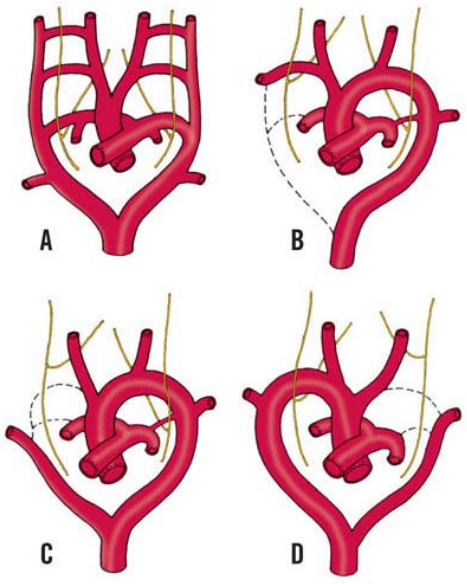
nerve, may be present in the presence of a variable right aortic arch. Another variation is presence of left subclavian artery behind oesophagus.

Recurrent laryngeal nerve in its lower course goes upward posterior to the pretracheal fascia with an angle to the groove. Nerve position itself in the groove in

its midcourse, where it may be medial to the ligament of Berry (suspensoory ligament of gland). It may lie in the ligament or in the gland itself.

Skamdalakis et al. Studied anatomy of bilateral recurrent laryngeal nerve of more than 100 cadavers. 50% of the specimen, anatomy of its position is in the groove. In the other 50% major nerves were coursing anteriorly or anterior to trachea or posterior to it. In very few cases nerve was found in the gland. Some other studies also showed smaller percentage of course of the nerve in thyroid.

Safest course of the recurrent laryngeal nerve is when its position of the groove where it appears least visible. Surgical morbidity is maximum when it courses the gland. Nerve should be identified and protected when it courses the suspensory ligament of the gland.



The recurrent laryngeal nerve traverses the main artery, the inferior thyroid artery. At the middle one third of thyroid, course may be variable as mentioned, anteriorly or posteriorly or may be even between division of the artery. Lekacos et al concluded that the majority of nerve course (above 80%) is posteriorly to or in between the division of artery that side. A study by Skandalakis et al concluded that on the right side, nerve most of the times lies beteen division of artery and on the left side, posterior to artery. Surgeon must be prepared for any anomaly as any variation may be expected here.

Sturniolo et al.128 emphasized that the secret to avoiding morbidity to the recurrent laryngeal nerve in surgical proccedures is as follows: (a) deep knowledge of the sical surgical anatomy of the thyroid region; (b) total extracapsular thyroidectomy; (c) a thorough search, identification, and exposure of the nerve itself; and (d) following the course of the nerve with care.

According to Procacciante and colleagues,129 after the recurrent laryngeal nerve is made taut by upward and medial traction of the thyroid, it may be palpated caudally to the inferior pole of the gland. This maneuver aided safe dissection in the region of the inferior thyroid artery.

Marchesi et al.130 reported an occurrence rate of 0.34% of inferior laryngeal nerve which is non recurrent on the right, and extreme rarity on the left side. They reported seven cases of nonrecurrent laryngeal nerve, and emphasize the diagnostic accuracy of angio-MR for the anatomic identification of the vascular anomaly that invariably occurs with the nerve malformation.

The nonrecurrent nerve (left or right, when present) may course to the larynx ithout any relation to the inferior thyroid artery or a loop may be formed around the subclavian artery.

Avisse et al.131 reported 17 cases of a right nerve which is non recurrent. In the study, in two cases an aberrant right subclavian artery coexisted with a non recurrent inferior laryngeal nerve.

Sanders et al.,132 who dissected out seven findings of laryngeal nerve which are non recurrent over 1000 thyroidectomies, reported the following:

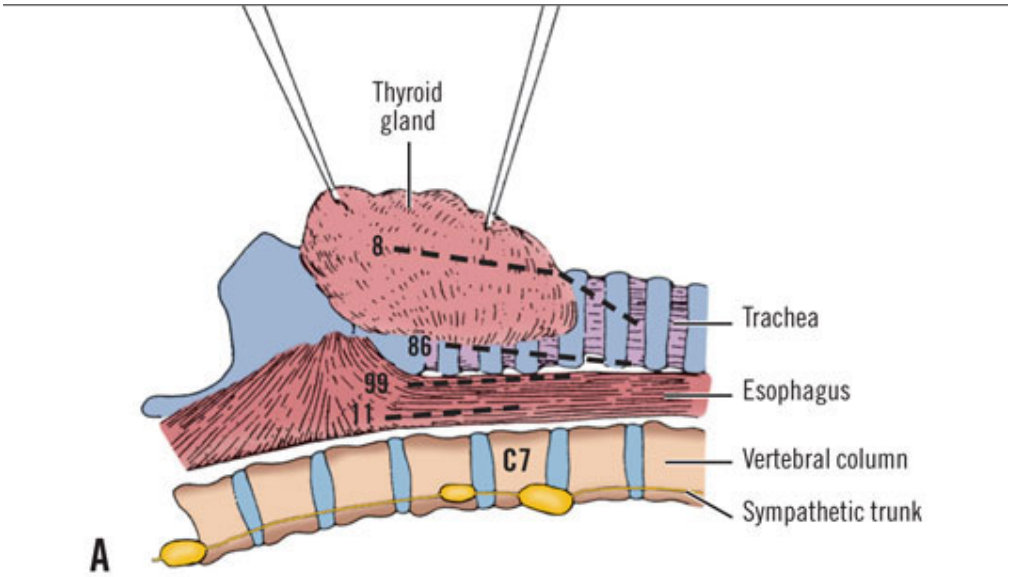
Out of these 7, in two cases, there were present both a non recurrent and in addition presence of a recurrent branch were made out on the right. This is a rare presentation which is not recorded before. The ignorance of this scenario, a surgeon may result in surgical morbidity. So such an observation may be well stressed and nerve should be completely identified in thyroidectomy.

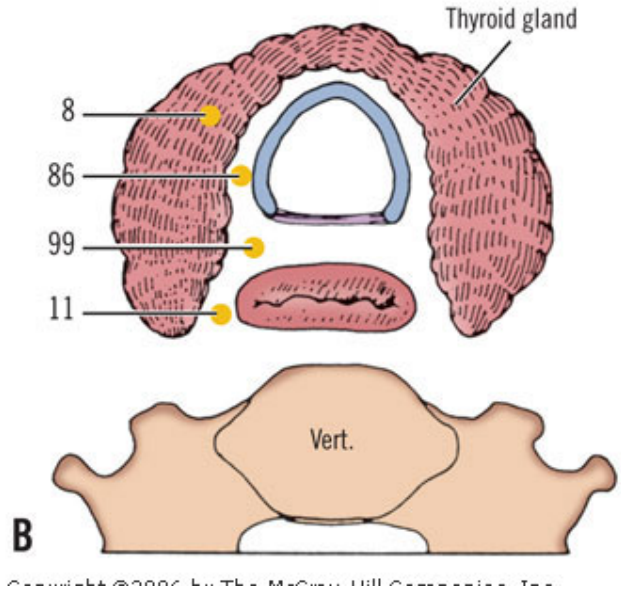
Miyauchi et al.133 reported good results with simple neurorrhaphy or with graft (vagus nerve - ansa cervicalis) of the injured recurrent nerve. Their 8 patients recovered from hoarseness, and maximum phonation improved. Steinberg et al.134 stated that branches of the recurrent laryngeal nerve (motor as well as sensory), together with sympathetic nerves, supply the larynx beneath the cords, pharynx, cervical oesophagus, and cervical trachea.

EXPOSURE:

Recurrent nerve should be readily exposed and visualised in any surgical procedure and should be precisely followed in all possible scenarios. In case nerve not identified, surgeon should be skillfull to avoid possible hidden areas and avoid injury. Fibrosis, increased bleeding, and lack of clear anatomic relationships are responsible for most nerve injuries. Postoperative exploration for hemorrhage also is associated with a higher risk of nerve injury.

A thorough exploration respecting the anatomy and sound knowledge of the anatomy of recurrent laryngeal nerves , its variation of courses in the neck , and striving to achieve perfect haemostasis at every step of surgery will greatly reduce the risk of injury





In the past, recurrent laryngeal nerve was deemed unfit for visualisation and dissection owing to its delicate and weak nature. It was supposed that visualisation by dissection may result in injury. And to the other hand, there was another school of thought, who stressed on visualisation and demonstration of recurrent laryngeal nerve by direct stimulation means during laryngoscopic observation. It should be stressed that identification should not involve unnecessary traction, stripping of fibrosed or normal connective tissue, compression which may injure nerve. Wholesome surgical dissection is unnecessary, but benign exposure will not injure it. From their investigation of 803 goitre operations and a literature search, Jatzko et al. noted a significantly higher rate of morbidity to the recurrent laryngeal nerve when it was not identified (5.2%) than when it was exposed (1.2%).

A triangle is mentioned in anatomy where the esteemed nerve discussed here forms the medial side or border, inferior thyroid artery forms superior border and common carotid forms lateral border. Inferior cornu of thyroid cartilage is a good landmark that the nerve enters larynx just postrerior to it. In case of a abscence, always a nerve which is nonrecurrent should be suspected.

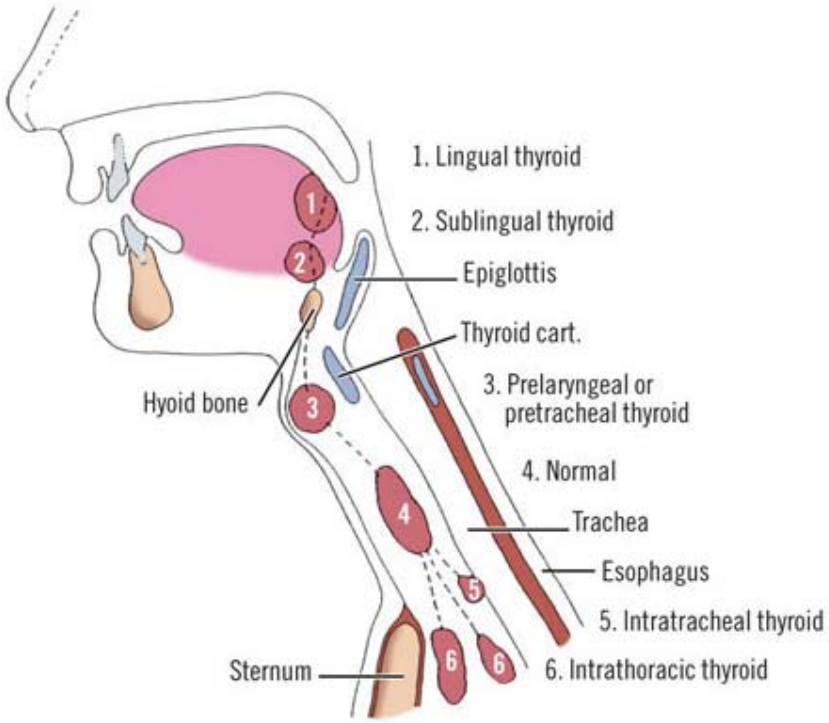
Pelizzo et al. advised that the best way to locate the recurrent laryngeal nerve during thyroidectomy is the Zuckerkandl's tuberculum, which is located on the lateral portion of each of the thyroid lobes, and according to these authors is the constant anatomic landmark when present

EMBRYOLOGY

Third week of life, thyroid starts its journey as it sprouts rom primitive foregut. Origin is from tongue base at a point also known as foramen caecum. Medial thyroid anlage which is formed from endodermal cells is present in the base of pharyngeal complex which traverse down neck in front to comlex anatomy that forms hyoid and larynx later. When it descends down, it joins with foramen caecum though a tubular embryological structure called the thyroglossal duct. Thyroid follicular cells are made by these epithelial cells of anlage. Fourth branchial pouch give rise to a pair of lateral anlage and this merges with medial anlage at later gestational period of 5 weeks. Ultimobranchial bodies are neuroectodermal in its embryological origin, give rise to parafollicular cells (C cells). It lies in superior and posterior position of the gland. By 8 weeks, thyroid follicles become obvious and by 11 th week colloid is formed.

DEVELOPMENTAL ANOMALY

LINGUAL THYROID:- Since path of thyroglossal duct arises from foramen caecum of tongue to the base of neck or somewhere above the arch of aorta. So this gland can develop anywhere in between the aforesaid.

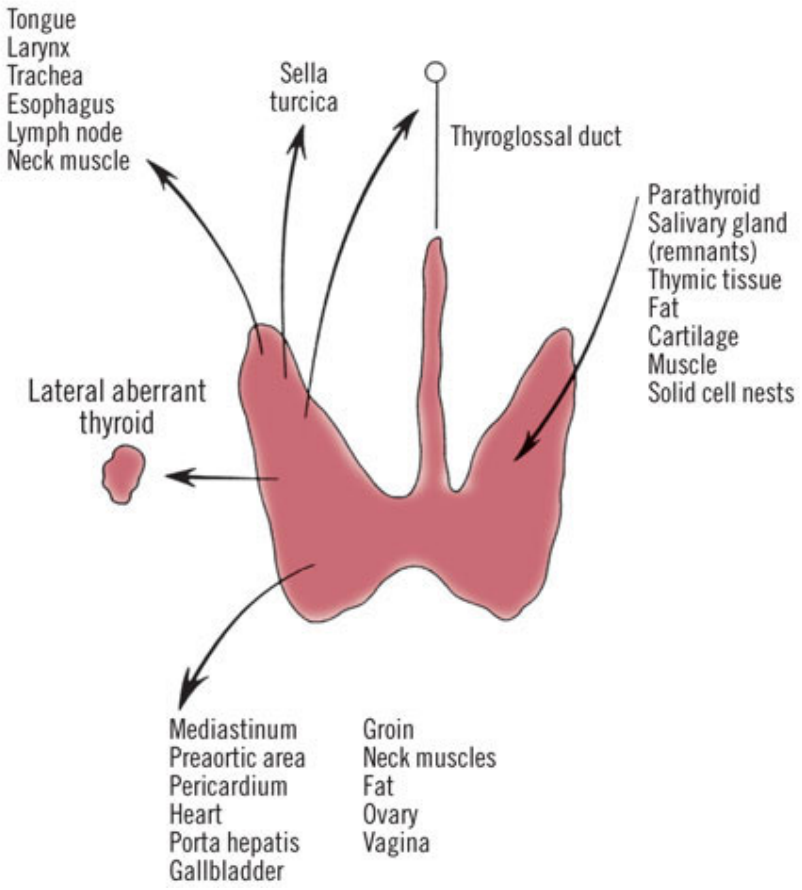


If thyroid tissue is only present in tongue and nowhere else, it is called as lingual thyroid. 2 out of 12 lingual thyroid is malignant. So it is important to excise the whole tissue. Afterwards, if frozen section of the excised tissue shows no malignant growth, then it can be re implanted in anterior abdominal wall.

PERSISTANT REMANANT OF THYROGLOSAL DUCT:

Foramen caecum and pyramidal lobe is normal remnant of thyroglossal duct. Thyroglossal cyst, thyroglossal fistula, which is very much prone for getting infected are major problems. Sistrunk procedure, that is foramen caecum, mid portion of hyoid bone, pyramidal lobe, all should be removed together.

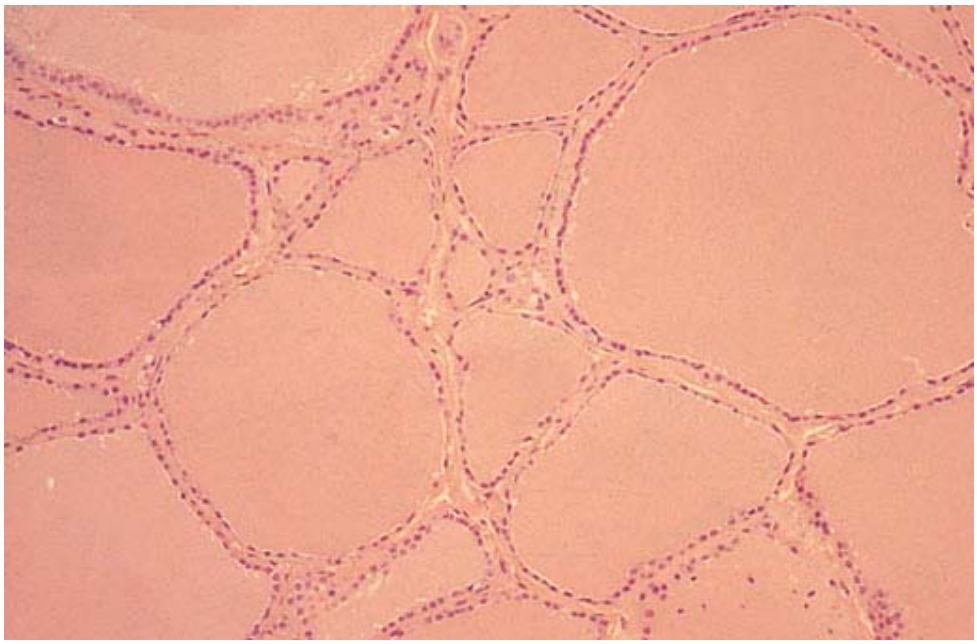
ACCESSORY ECTOPIC THYROID TISSUE:- Can be clearly directed through this picture.



HISTOLOGY

The thyroid gland is surrounded by the capsule, which is a feeble layer of fibrous connective tissue. Sprung out from capsule, several septa extend within the thyroid parenchyma, which is subdivided into several lobules. Epithelial cells (cuboidal or squamous) form the thyroid follicles; they are separated by thin connective stroma which is rich in both lymphatic and blood vessels. Small bundles of nerves are present.

There is a colloidal gelatinous collection in the center of the follicle. Each follicle has two types of cells: follicular and parafollicular, or C cells.



According to Ross and Reith,152 the follicular cells are responsible for the following actions: synthesis of thyroglobulin, iodination, storage of thyroglobulin, resorption of thyroglobulin, hydrolysis of thyroglobulin, and release of thyroid hormone into the blood and lymphatics.

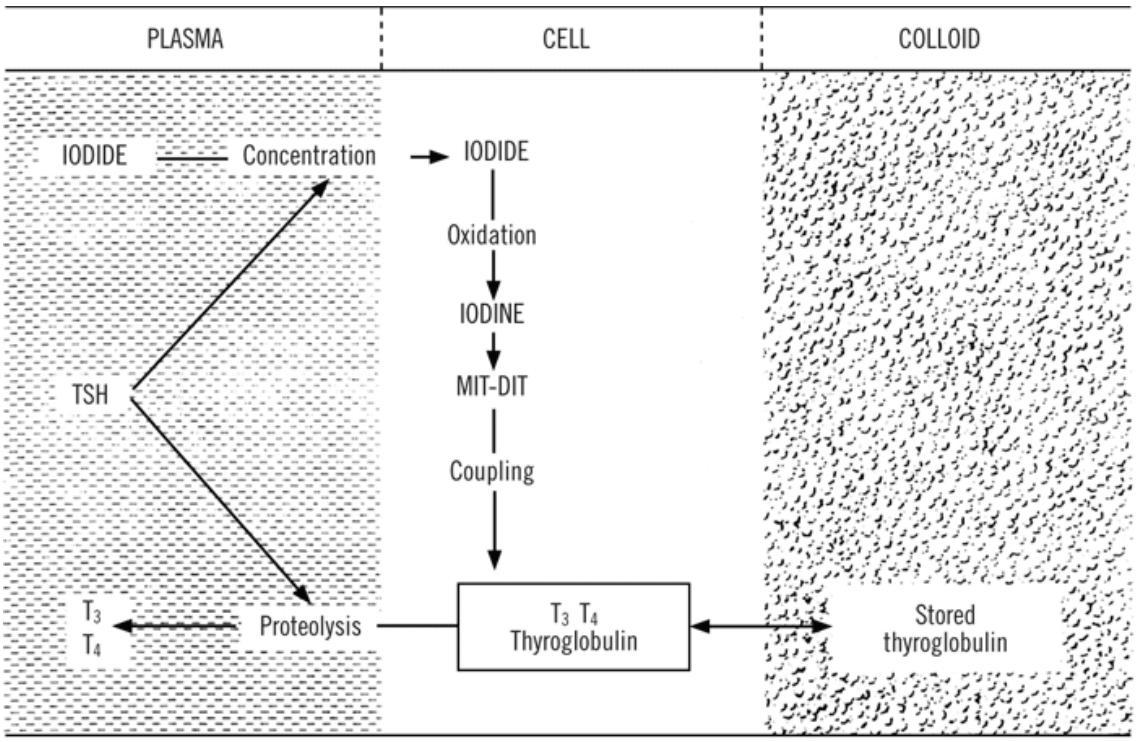
The parafollicular, or C cells, can be found in the connective stroma between the follicles or in the follicular epithelium. Characteristically, they contain several secretory granules.

Thyroglobulin, an iodinated glycoprotein, is stored in thyroid follicles.Thyroglobulin is the storage form of thyroxine (T_4) and tri-iodothyronine (T_3). The thyroid follicles are lined by epithelial cells which are responsible for the synthesis of the glycoprotein component of thyroglobulin and for the conversion of iodide to iodine. When active thyroid hormone is required, the thyroid epithelial cells remove some of the stored thyroid colloid and detach T_3 and T_4, which pass through the cell into an adjacent capillary. When inactive, these cells are simple flat or cuboidal cells, but when active they are tall and columnar.

PHYSIOLOGY

Synthesis of thyroxin.

{ TSH- thyroid stimulating hormone; MIT- Monoidothyrosine; DIT- diidothyrosine; T4- thyroxine; T3- triidothyronine}



Ingested iodides are utilised in stomach and upper duodenum and proximal jejunum and inorganic iodide, almost removed from the plasma at a rate of 10 mg/h through a process of active transport into thyroid follicular cells. Inorganic

iodide attaches to a specific thyroid peroxidase at the apical (luminal) aspect of the follicular cell which also represents a binding site for tyrosine residues on thyroglobulin. Both the iodide and tyrosine are oxidized by the peroxidase enzyme to form mono-iodotyrosine which is in bulk and di-iodotyrosine which is in small percentage. On thyroglobulin procedure, coupling of mono-iodotyrosine and di-iodotyrosine molecules occurs through the action of peroxidase and transaminase resulting in the synthesis of T3 (mono-iodotyrosine + di-iodotyro-sine) or T4 (di-iodotyrosine + di-iodotyrosine).

Thyroglobulin with its associated thyroid hormones is reabsorbed from the colloid by endocytosis into the apical aspect of the thyroid follicular cell. Thyroglobulin is then hydrolysed by peptidases within lysosomes and free thyroid hormones released by diffusion into capillaries from the basal surface of the cell. Small quantities of thyroglobulin are also released during this process while mono-iodotyrosine and di-iodotyrosine molecules are deiodinated and degraded to release iodine and tyrosine which are recycled.

EFFECTS OF THYROXIN

METABOLISM:-

It increases the rate of glycolysis, gluconeogenesis, and increase uptake of glucose from gut. Thereby, secondarily increases insulin secretion.

Mobilisation of fatty acid from adipose tissue increase the concentration of fatty acid in blood and increase the rate of fat metabolism.

It also decreases the concentration of lipids, cholesterol and triglyseride in blood plasma and vice versa.

CARDIOVASCULAR SYSTEM:-

In physiology, it increases the rate of blood flow as well as cardiac output to 60%.

Heart rate is increased by excess of hormone and decreased by its deficiency.

Mild increase of throxine causes increase in cardiac muscle strength but on contrary hyperthyroidism causes weakness of heart muscle by increasing proteolysis.

Mean arterial pressure does not change but pulse pressure increases much since systolic pressure increases by 10-15 and the diastolic pressure falls.

RESPIRATORY SYSTEM:-

Respiratory rate increases because of increased yield of metabolite by products.

AERO-DIGESTIVE SYSTEM:-

Hyperthyroidism leads to diarrhoea and hypothyroidism causes constipation.

CENTRAL NERVOUS SYSTEM:-

In CNS, hyperthyroidism causes anxiety complex, paranoia, stress, tiredness.

Muscle tremors is the most common sign illustrated in female hyperthyroidism. It is due to increased reactivity to neuronal synapses.

REPRODUCTIVE SYSTEM:-

In menses, hypothyroidism causes oligomenorrhoea and in hyperthyroidism it causes menorrhagia.

PATHOLOGY

Classification of thyroid diseases

I. Diseases associated with thyrotoxicosis

1. Graves' disease

2. Toxic nodular goitre a) Toxic adenoma b) Toxic multinodular goitre

3. Thyroiditis

4. TSH secreting pituitary tumors

5. hCG induced hyperthyroidism e.g. gestational, trophoblastic disease associated

6. Iodine induced hyperthyroidism e.g. iodine, Amiadarone

7. Thyrotoxicosis factita

II. Diseases associated with hypothyroidism

1. Goitrous hypothyroidism e.g. Hashimoto's thyroiditis, iodine deficiency, lithium deficiency

2. Congenital hypothyroidism

3. Atrophic hypothyroidism: e.g. Hashimoto's thyroiditis, post ablative

4. Central hypothyroidism

III. Euthyroid

1. Diffuse nontoxic (simple) goitre

2. Nodular thyroid disease e.g. solitary nodule, multinodular goitre

3. Thyroid neoplasia: e.g. follicular adenoma, thyroid malignancy

HYPERTHYROIDISM

Treatment of thyrotoxicosis was described by Cecil Joll, a surgeon from London. He did subtotal thyroidectomy even in late 1930s.

Thyrotoxicosis is the state of symptomatic thyroid hormone excess, of both endogenous and exogenous cause. It is not synonymous with hyperthyroidism, which is the result of excessive thyroid function.

Increased levels of T4 and T3 results in hypermetabolic state strictly termes as thyrotoxicosis. Hyperthyroidism is caused by increased superadded function of thyroid gland. In some cases, there is increase supply or increased release of thyroid hormones which are preformed, as seen in thyroiditis, sometimes source can be extra thyroidal. Hyperthyroidism is only one cause of thyrotoxicosis if we strictly follow the literature.

CLINICAL FEATURES

Signs & Symptoms of hyperthyroidism

General

Weight loss

Fatigue, apathy

Sweating, heat intolerance

Cardiovascular

Palpitations, dyspnoea, angina

Cardiac failure

Sinus tachycardia, atrial fibrillation

Collapsing pulse

Neuromuscular

Nervousness, agitation

Tremor, choreoathetosis

Psychosis

Muscle weakness, proximal myopathy

Periodic paralysis

Myasthenia gravis

Gastrointestinal

Weight loss despite increased appetite

Diarrhoea, steatorrhoea

Vomiting

Reproductive

Oligomenorrhoea

Infertility

Dermatological

Pruritus

Palmar erythema

Pretibial myxoedema*

Thinning of hair

Goitre

Diffuse with or without bruit*

Nodular

Ocular

Lid retraction, lid lag

Periorbital puffiness*

Increased lachrymation and grittiness of eyes*

Chemosis (conjunctival oedema)*

Proptosis, corneal ulceration*

Ophthalmoplegia, diplopia*

Papilloedema, loss of visual acuity*

***Features of Graves' disease alone**.

Weight loss which cannot be explained with an increased appetite attributed to increased metabolic rate is caused by thyrotoxicosis.

Weight gain occurs in 5% of patients, however, because of increased food intake. Other prominent features include hyperactivity, nervousness, and irritability, ultimately leading to a sense of easy fatigability in some patients.

Insomnia and impaired concentration are common; apathetic thyrotoxicosis may be mistaken for depression in the elderly. Fine tremor is a frequent finding, best elicited by having patients stretch out their fingers while feeling the fingertips with the palm.

Common neurologic manifestations include hyperreflexia, muscle wasting, and proximal myopathy without fasciculation. Chorea is rare. Thyrotoxicosis is sometimes associated with a form of hypokalemic periodic paralysis; this disorder is particularly common in Asian males with thyrotoxicosis, but it occurs in other ethnic groups as well.

The skin is usually warm and moist, and the patient may complain of sweating and heat intolerance, particularly during warm weather. Palmar erythema, onycholysis, and, less commonly, pruritus, urticaria, and diffuse hyperpigmentation may be evident. Hair texture may become fine, and a diffuse alopecia occurs in up

to 40% of patients, persisting for months after restoration of euthyroidism.

Gastrointestinal transit time is decreased, leading to increased stool frequency, often with diarrhea and occasionally mild steatorrhea.

Women frequently experience oligomenorrhea or amenorrhea; in men, there may be impaired sexual function and, rarely, gynecomastia.

The direct effect of thyroid hormones on bone resorption leads to osteopenia in long-standing thyrotoxicosis; mild hypercalcemia occurs in up to 20% of patients, but hypercalciuria is more common. There is a small increase in fracture rate in patients with a previous history of thyrotoxicosis.

In secondary thyrotoxicosis the goitre is nodular. The onset is insidious and may present with cardiac failure or atrial fibrillation. It is characteristic that the hyperthyroidism is not severe. Eye signs other than lid lag and lid spasm (due to hyperthyroidism) are very rare.

MYOPATHY

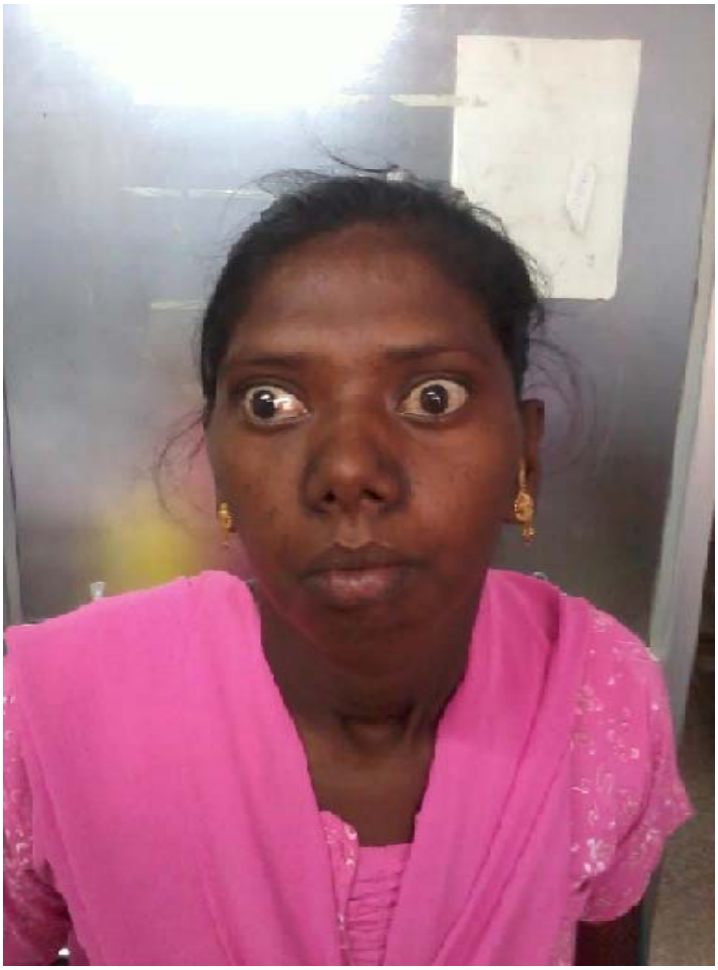
Weakness of proximal muscles, which recovers as the hyperthyroidism is controlled.

OPTHALMOPATHY

LID RETRACTION occurs by the increased sympathetic tone of levatar palpabrae supirioris which is partially supplied by sympathetic nerves. It can be controlled by drugs.

EXOPTHALMUS to varying degree even unilateral has been observed. True exophthalmos is a proptosis of the eye, caused by infiltration of the retrobulbar tissues with fluid and round cells, with a varying degree of retraction or spasm of the upper eyelid.

Presence of eyelid oedema, redness of conjunctiva and chemosis are increased when ophthalmic veins are compressed. Diploplia is resulted by weak action of extraocular muscles which is very apparent in severe hyperthyroidism.



CLINICAL EYE SIGNS:-

LID RETRACTION:-

Due to over sympathetic activity Levator Palpebae Superioris, the upper lid remains higher than normal and the lower lid remains at normal position. In general, the upper lid covers 5mm of cornea and lower lid just touches the lower margin. But in lid retraction, upper margin is also visible. LID LAG is just upper lid cannot keep pace with eye movement.

EXOPTHALMOS:-

With the retrobulbar tissue edematous oe inflamed the whole eye ball will pushed outside thereby retracting the eyelids. This is exopthalmus.

VON GRAEFFE'S SIGN:- upper eyelid lags behind when patient is asked to look downwards.

JOFFROY'S SIGN:- patient facing downwards and asked to look upwards, normally forehead will wrinkle but when it not, it is names as the sign.

STELLWAG'S SIGN:- starring look with infrequent blinking.

MOEBIUS' SIGN:- palsy of medial rectus leading to inability to converge eye.

DALRYMPETE'S SIGN:- upper part of sclera is visible due to lid retraction.

OPTHALMOPLEGIA:-

Due to muscle infiltration the upper and lateral rectus along with inferior oblique are paralysed. Therefore, inability to look uoward and outward.

CHEMOSIS:-

Due to increased retro bulbar pressure, the venous and lymph drainage is obstructed, thereby, collection of interstitial fluid causing edema in conjunctiva. This is called as chemosis of eye.

CARDIAC CYCLE:-

Even during sleep there is tachycardia, which is defined as sleeping pulse rate. Arrhythmia are superimposed. There are various stages in the evolution of thyrotoxic cardioarrythmias:

1 multiple extrasystoles;

2 paroxysmal atrial tachycardia;

3 paroxysmal atrial fibrillation;

4 persistent atrial fibrillation, not responsive to digoxin.

DERMATOPATHY:-

Thyroid dermopathy (‘**pretibial myxoedema’**) is a rare condition characterised by thickening of the skin, usually in areas of trauma, by deposition of hyaluronic acid in the dermis and subcutis. It usually occurs a few years after the onset of thyrotoxicosis and usually responds to treatment of the underlying thyroid disorder and topical steroids.

DIAGNOSIS

'TRH' is the immune assay of thyroid stimulating hormone(TSH), which tend to decrease in hyperthyroidism and free T4 level will increase. In some cases free T3 level increases. In secondary hyperthyroidism, Thyroid Releasing Hormone (TRH) is administered and usual rise is TSH in relation to TRH excludes out secondary hyperthyroidism. Second step will be Radioactive Iodine Uptake scan will be helpful on diagnosis. For example diffusely increased uptake in the whole gland (Graves' disease), increased uptake in a solitary nodule (toxic adenoma), or decreased uptake (thyroiditis).

PATHOLOGY

Some disturbance in thyroid hormone synthesis leads to increased productions of thyroid stimulating hormones thereby increasing the functional mass of thyroid gland. This is more like compensatory increase to overcome the decreased production of thyroxin. So diffuse swelling appears in thyroid gland, clinically thyroid is never palpable in ordinary conditions but if we can make out the feel of thyroid as a whole then it is diffuse swelling.

Almost all the long standing diffuse swelling changes to mutinodular goitre. Clinically, if at least one nodule is palpable along with diffuse gland swelling then it is cut off line to diagnose Multi Nodular Goitre.

Morphology of MNG:- multilobulated, asymmetrically enlarged, progressive enlargement is highly unpredictable. Weather, it would affect one side only or both lobes. Its tremendous growth gives contact pressure on adjacent structures , like trachea and oesophagus. Also it can grow behind sternum and cause mass compression leading to SVC compression syndrome. It is checked by PEMBERTON sign, by rising both upper limbs and examine for 1min. Facial conjunctiva congestion with dilated veins mark the SVC compression.

On cut section : nodules with variable size with brown coloured gelatinous colloid filled. It may have area of haemorrhage, fibrosis, calcification, cyctic changes, but most common in older land long standing goitre. Epithelium which are inactive and flattened lining colloid rich follicles with patches of follicular hyperplasia along with changes that are degenerative in certain areas are a classical microscopic appearance.

GRAVES DISEASE:-

"Violent and long continued palpitation in female" is characteristic of

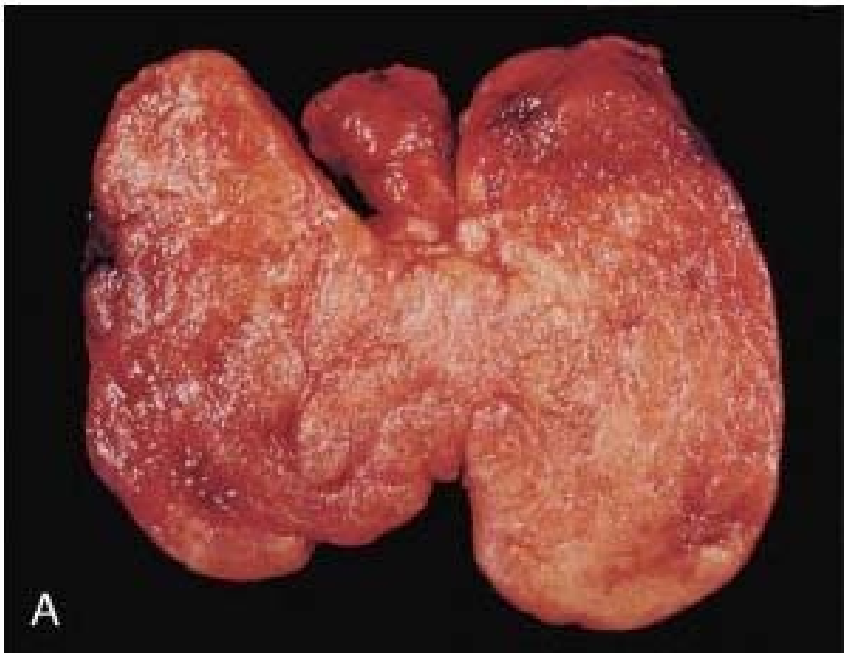
graves disease. It is most common cause of endogenous hyperthyroidism defined by

1. Hyperthyroidism
2. Opthalmopathy
3. Demopathy or pretibial edema.

It is basically autoimmune disease leading by production of many types of antibody.

1. Thyroid-Stimulating antibody- it is of IgG type, by binding to TSH receptors it mimics its function. This will be present in almost all the grave disease patient.
2. Thyroid Growth Stimulating Immunoglobulin: it also works on TSH receptor.
3. TSH Binding Inhibitor immunoglobulin:- it actually inhibit the TSH to bind to TSH receptor and also function as TSH hormone itself or in reverse it can cause hypothyroidism.

MORPHOLOGY:-



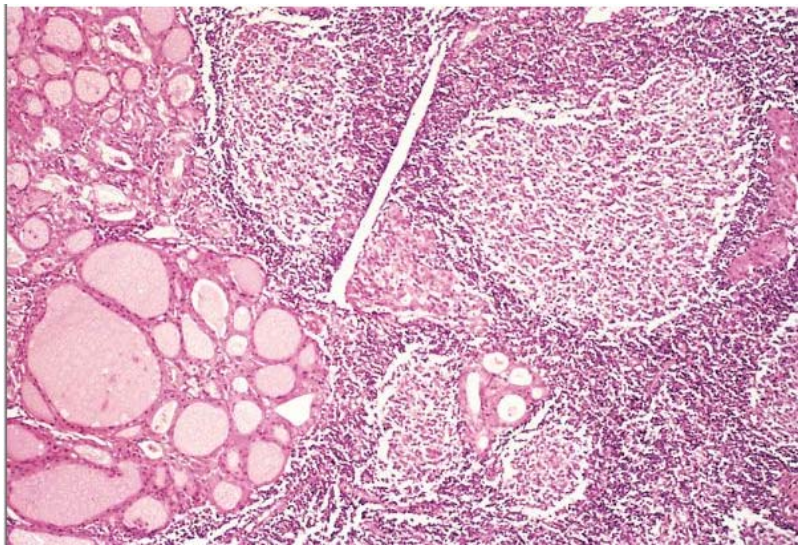
It is diffusely enlarged. On cut section, the parenchyma has a soft, meaty appearance resembling normal muscle. Microscopically the follicular epithelial cell much more crowded that sometimes it forms a papilla which dips in lumen of follicle. Lymphoid infiltrates, consisting predominantly of T cells, with fewer B cells and mature plasma cells, are present throughout the interstitium; germinal centers are common.

Hasimoto Thyroiditis:- it is autoimmune disorder leading to hypothyroidism most common cause of hypothyroidism in area of fair availability of iodine.

It is also called as struma lymphomatosa because of presence of lymphocytes. Basically two types of antibodies are present, first one anti-peroxidase and second one is anti-thyroglobulin. Induction of thyroid autoimmunity is accompanied by a progressive depletion of thyrocytes by apoptosis and replacement of the thyroid parenchyma by mononuclear cell infiltration and fibrosis. Various methods of cell death are:

1. CD8+ cytotoxic T cell mediated cell death.
2. Cytokine mediated cell death.
3. Binding of antithyroid antibody followed killer cells.

Morphology:



Diffusely enlarged or more often localised enlarged, capsule is well intact, the cut surface is pale yellow tan, firm and somewhat nodular. Microscopically parenchyma is highly populated with mononuclear inflammatory infiltrates. Many area the epithelial lining follicle is lined by more dense eosinophilic cytoplasm containing cell called as Hurthle cell.

SUBACUTE GRANULOMATOUS THYROIDITIS:

Triggering factor is viral infection. Most patient complaint of upper respiratory tract infection followed by thyroiditis. Mostly occurs by seasonal variation and associated with coxsackievirus, mumps, measles, adenovirus, and other viral illnesses.

Morphology: gland may be unilateral or bilaterally enlarged with intact capsule, slightly attached to surrounding tissues. Cut surface is firm and yellow white, more rubbery and brown. Early in the active inflammatory phase, scattered follicles may be entirely disrupted and replaced by

neutrophils forming microabscesses. Later, the more characteristic features appear in the form of aggregates of lymphocytes, activated macrophages, and plasma cells about collapsed and damaged thyroid follicles. Multinucleate giant cells enclose naked pools or fragments of colloid, hence the designation granulomatous thyroiditis.

SUACUTE LYMPHOCYTIC (PAINLESS) THYRODITIS: it comes to attention by painless goiterous growth, most commonly it occurs in postpartum stage. Two variants of graves disease is postpartum thyroiditis and subacute lymphocytic thyroditis. Being an autoimmune disease it carries anti peroxidise antibody.

Morphology. Except for possible mild symmetric enlargement, the thyroid appears normal on gross inspection. The most specific histologic features consist of lymphocytic infiltration with hyperplastic germinal centers within the thyroid parenchyma and patchy disruption and collapse of thyroid follicles. Unlike in frank Hashimoto thyroiditis, however, fibrosis and Hürthle cell metaplasia are not prominent features.

SOLITARY NODULE:

A solitary nodule is having more chance of malignancy if in males.

A solitary nodule is having more chance of malignancy that multinodular.

Young patient with solitary nodule is having more chance of malignancy.

History of radiation treatment of head and neck is having more chance.

Functional nodue (hot nodule) are expected to be more benign.

Benign neoplasms outnumber thyroid carcinomas by a ratio of nearly 10 : 1. While under 1% of solitary thyroid nodules are malignant.

ADENOMAS:

Discrete, solitary masses, derived from follicular epithelium, and hence they are also known as follicular adenomas. A small proportion produces thyroid hormones and causes clinically evisent thyrotoxicosis. Toxic adenomas are independent of TSH, it one of the example of thyroid autonomy.

Somatic mutations of the TSH receptor signaling pathway have been found culprit in toxic adenomas, as well as in toxic multinodular goiter. Gain-of-function mutations in one of two components of this great signaling system—most often TSHR itself or the α-subunit of Gs (GNAS)—allow follicular cells to secrete thyroid hormone independent of TSH stimulation ("thyroid autonomy"). This causes symptoms of hyperthyroidism and produces a "hot" thyroid nodule on imaging.

Morphology:

solitary, spherical, encapsulated lesion, average size 3cm, but max size 10cm, bulges from the cut surface and compresses the adjacent thyroid. The color ranges from gray-white to red-brown, depending on the cellularity of the adenoma and its colloid content. The neoplastic cells are demarcated from the adjacent parenchyma by a well-defined, intact capsule. Areas of hemorrhage, fibrosis, calcification, and cystic change, similar to those encountered in multinodular goiters, are common in follicular adenomas, particularly within larger lesions.

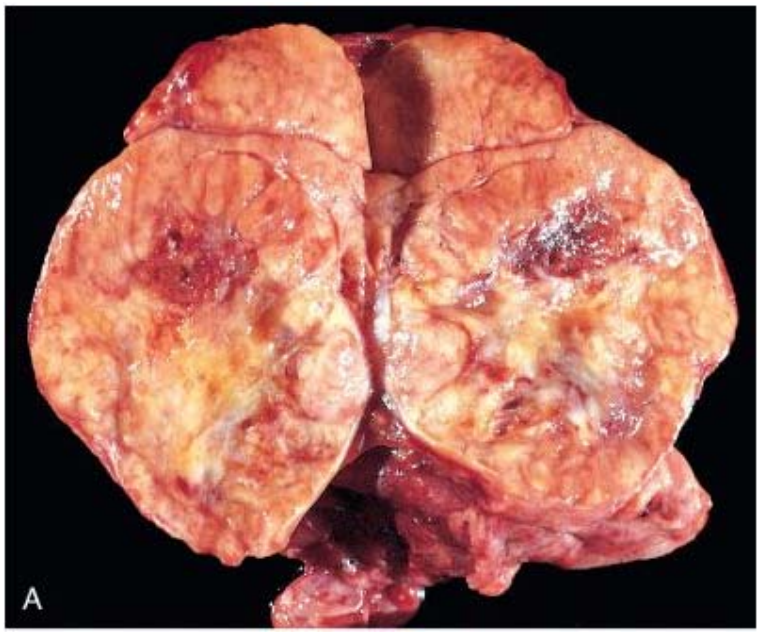
CARCINOMA:

Most of the carcinomas are epithelial in origin except for medullary carcinoma. Types are.

1. Pappilary carcinoma (>85%),
2. Follicular carcinoma(5-15%),
3. Anaplastic carcinoma(<5%),
4. Medullary carcinoma(5%).

PAPPILRY CARCINOMA: Solitary or multifocal lesion, they infiltrate surrounding parenchyma with ill defined margins, it may fe firotic, hemorrhagic or even cystic in appearance. Cut surface sometimes reveals pappilary surface.

FOLLICULAR CARCINOMA: single nodules that may be well circumscribed or widely infiltrative. Lesions may penetrate the capsule and infiltrate well beyond the thyroid capsule. Gray to tan to pink on cut section and, on occasion, are somewhat translucent.



ANAPLASTIC CARCINOMA:

Composed of highly anaplastic cells, with variable morphology, including: (1) large, pleomorphic giant cells, including occasional osteoclast-like multinucleate giant cells; (2) spindle cells with a sarcomatous appearance; and (3) mixed spindle and giant cells. The neoplastic cells express epithelial markers like cytokeratin, but are usually negative for markers of thyroid differentiation, like thyroglobulin.

MEDULLARY CARCINOMA: it of neurendocrinal in origin from parafollicular or otherwise calles as C cells. This C cells secreats calcitonin , an important

marker we use in post operative cases. 70% it is sporadic but rest of it occurs in association of MEN 2A and 2B syndrome.

MORPHOLOGY: firm, pale gray to tan, and infiltrative. There may be foci of hemorrhage and necrosis in the larger lesions, sporadic cases are basically solitary nodular but with MEN it appears with bilaterally enlarged with nodules.

OTHER GRADING SYSTEMS

CLINICAL ACTIVITY SCORE:- It was devised in the year of 1997, for graves opthalmopathy, widely used for the judgement of therapeutic outcome of the disease. Basically, graves opthalmopathy is a biphasic disease. First phase defined by active inflammation and the second as a burnt out stage with stable proptosis and muscle weakness. Functionally, the scoring criteria is based on four basic signs, Pain, redness , swelling and impairment of function.

Pain	1	Painful, oppressive feeling on or behind the globe during the last 2 weeks
	2	Pain on attempted up, side or down gaze during the last 4 weeks
Redness	3	Redness of the eyelids
	4	Diffuse redness of the conjunctiva covering at least one quadrant
Swelling	5	Swelling of eyelids
	6	Chemosis
	7	Swollen caruncle
	8	Increase of proptosis ≥2 mm during a period of 1-3 months
Impaired function	9	Decrease of eye movements in any direction ≥5° during a period of 1-3 months
	10	Decrease of visual acuity of ≥1 line on the Snellen chart (using a pin hole) during a period of 1-3 months

The score may vary from 0 to 10. Conclusively, as high the score more responsive for immunosuppressive drugs. Score >4 suggest active inflammatory stage of graves opthalmopathy. CAS score do not differ in duration of disease mostly it remains constant. Sensitivity of the scoring system is around 55%.

This system is able to predict the therapeutic outcome based on clinical signs and symptoms. High risk of inter observer variation.

NOSPECS system have been used for more than an decade. It uses the signs involving soft tissue, corneal involvement and sight loss. It is more useful to assess the progression of disease. The benefit we get is minimal inter-observer variability.

Score	Grade	Change
0		No signs and symptoms
1		Only Signs
2		Soft tissue involvement, with symptoms and signs
o	Absent	
a	Minimal	
b	Moderate	
c	Marked	
3		Proptosis
o	<23 mm	
a	23-24 mm	
b	25-27 mm	
c	≥28 mm	
4		Extraoccular muscle involvement
o	Absent	
a	Limitation of motion in extremes of gaze	
b	Evident restriction of movement	
c	Fixed eye ball	
5		Corneal involvement
o		Absent
a	Stippling of cornea	
b	Ulceration	
c	Clouding	
6		Sight loss
o	Absent	
a	20/20- 20/60	
b	20/70- 20/200	
c	<20/200	

Furthermore, NOSPECS is itself a mnemonic which helps medical students to learn the signs of graves' disease.

BILLEWICS SCORE for HYPOTHYROIDISM. In era of lack of advanced investigative facilities, this criteria was used to diagnose hypothyroidism. It utilises 6 sign and 8 symptoms to asses thyroid state. The final score may vary from +67 to – 47.

	Present	Absent
Symptom		
Diminished sweating	+ 6	- 2
Dry skin	+ 3	- 6
Cold intolerance	+ 4	- 5
Weight increase	+ 1	- 1
Constipation	+ 2	- 1
Hoarseness	+ 5	- 4
Deafness	+ 2	0
Signs		
Slow movements	+ 11	- 3
Coarse skin	+ 7	- 7
Cold skin	+ 3	- 2
Periorbital puffiness	+ 4	- 6
Pulse rate	+ 4	- 4
Ankle jerk	+ 15	- 6

The best part of the score system is, it comes along the methodology of how to examine the signs to decrease the inter—observer variation. For example,

decreased sweating is asses in centrally heated hall. Dry skin is significant only when it is required medical treatment. Cold intolerance can be judged as the patients preference for warm room, extra bed clothing. Weight increase is significant only when patient complaints of tightness of clothing. The symptom of constipation is significant only when patient is using laxatives. Hoarseness of voice checked by speaking as well as singing voice. Paraesthesia is a subjective sensation.

Slow movement is checked by observing the patient changing the buttoned garments. Cold skin is assessed by comparison between the the skin of patient and that of examiner. Periorbital puffiness is significant if it is hindering the malor curves. Billewics suggested to count the pulse for 30s and less than 30 is suggestive of braydicardia. The method of ankle jerk is by placing knee on chair and grasping the chair. A score of 25 or plus is suggestive of hypothyroidism or score less than -30 excludes the disease.

ZULEWSKY SCORE for HYPOTHYROIDISM- it assess thyroid function, tissue thyroid status and clinical signs. The tissue thyroid status is judged by Ankle relaxation time (ART) and total cholesterol.

On the basis of			New score	
			Present	Absent
Symptoms				
1	Diminished sweating	Sweating in the warm room or a hot summer day	1	0
2	Hoarseness	Speaking voice, singing voice	1	0
3	Paraestheisa	Subjective sensation	1	0
4	Dry Skin	Dryness of skin, noticed spontaneously, requiring treatment	1	0
5	Constipation	Bowel habit, use of laxative	1	0
6	Impairment of hearing	Progressive impairment of hearing	1	0
7	Weight increase	Recorded weight increase, tightness of clothes	1	0
Physical signs				
1	Slow movements	Observe patient removing his clothes	1	0
2	Delayed ankle reflex	Observe the relaxation of the reflex	1	0
3	Coarse Skin	Examine hands, forearms, elbow for roughness and thickening of skin	1	0
4	Peritorbital puffiness	This should obscure the curve of the malar bone	1	0
5	Cold skin	Compare temperature of hands with examiner's	1	0
Sum of all symptoms and signs present			12	0

But the main clinical scoring is the same of Billewics score system, all it adds is the ART.

TIRADS (Thyroid Imaging Reporting and Data System- it classify thyroid nodules into 6 categories. This grading system is used to avoid unnecessary interventional procedures.

Description of US pattern	US patterns	Malignancy	TIRADS
Anechoic with hyperechoic spots, nonvascularized lesion	Colloid type 1		
Nonrncapsulated, mixed, nonexpansile with hyperechoic spots, vascularized lesion, "grid" aspect (spongiform nodule)	Colloid type 2	0%	TIRADS 2: benign findings
Nonrncapsulated, mixed with solid portion, isoechogenic, expansile, vascularized nodule with hyperechoic spots	Colloid type 3		
Hyper-, iso-, or hypoechoic, partially encapsulated nodule with peripheral vascularization, in Hashimoto's thyroiditis	Hashimoto pseudonodule	5%	TIRADS 3: probably benign
Solid or mixed hyper-, iso-, or hypoechoic nodule, with a thin capsule	Simple neoplastic pattern	5-10%	TIRADS 4A: undetermined
Hypoechoic lesion with ill-defined borders, without calcifications	de Quervain pattern		
Hyper-, iso-, or hypoechoic, hypervascularized, encapsulated nodule with a thick capsule, containing calcifications (coarse or microcalcifications)	Suspicious neoplastic pattern		
Hypoechoic, nonencapsulated nodule, with irregular shape and margins, penetrating. Vessels, with or without calcifications	Malignant pattern A	10-80%	TIRADS 4B: suspicious
Iso- or hypoechoic, nonencapsulated nodule with multiple peripheral microcalcifications and hypervascularization	Malignant pattern B	>80%	TIRADS 5: consistent with malignancy
Nonencapsulated, isoechoic mixed hypervascularized nodule with or without calcifications, without hyperechoic spots	Malignant pattern C cancer, confirmed by the previous biopsy	100%	TIRADS 6: malignant

TIRADS 2 signifies benign findings; TIRADS 3 is probably benign, while TIRADS 4A and 4B represent undetermined and suspicious findings respectively. An imaging picture consistent with malignancy is graded as TIRADS 5, while TIRADS 6 represents confirmed malignancy.

METHODOLOGY

PERIOD OF STUDY- September 2012 TO SEPTEMBER 2013

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria- patient with symptoms suggestive of hyperthyroidism or neck swelling admitted in tvmch over duration of one year is being considered for the study.

Inclusion criteria:-

Age > 12years

Previously diagnosed to be a case of thyroid

Patient with thyroid swelling

Exclusion criteria:-

Age <12

Known serior medical co-morbidity

Pregnancy

Indicator consideredin the study are those mentioned in the criteria.

A through history, clinical examination and investigations are carried out.

Outcome measures:-

Wayne's diagnostic criteria as an aid to diagnose hyperthyroidism.

Its utility is explained by theclinical fatures.

Statistical analysis:-

The statistical analysis is done by using method of central tendency(mean median, mode), Chi-square test and data packages.

SAMPLE SIZE- 53

OUTCOME AND MEASUREMENT-

Cases was examined investigated and followed from date of admission to date of discharge as well as in follow up period. Following criteria was followed.

Name

Age

Sex

Address

IP/OP number

Date of admission/ Visit

Date of discharge

H/ O Swelling at the base of neck.

H/O Pain

H/O Pressure Effect – Dysphagia, Hoarsness of voice, Dysphonea, Stridor.

Symptoms- loss of weight, preference to cold, excessive sweating, nervous, irritability, insomnia, tremor of hand, weakness of muscle, palpitation, dyspnoea on exertion, exopthalmus, staring gaze. Diplopia, chemosis, amenorrhoea.

Symptoms of secondary thyrotoxicosis.- palpitation, chest pain, signs of cardiac failure

Past history-

Personal history- of dilatory habit and menstruation, bladder and bowel habit.

General survey-

Built and Nourishment-

Facies-

Mental status-

Skin- hot and moist palms

LOCAL EXAMINATION.

THYROID SWELLING WILL BE AT THE BASE OF NECK, MOVES WITH DEGLUTATION, DOES NOT MOVES WITH PROTRUSION OF TONGUE,

PALPATION- Lahey's method, Crile's method, Kocher's test, pemberton sign. . palpation of cervical lymph node.

General Examination-

Primary Toxic manifestations

Eye signs- lid retraction, exopthalmus, Von Graefe's sign, Joffroy's sign, Stellwag sign, Moebius sign, Dalrympte's sign

Opthalmoplegia- weakness of superior and lateral restus

Chemosis of eye.

Tachycardia

Tremors

Moist skin

Thyroid Bruit

Secondary Toxic Manifestations

Cardiovascular system mainly effected, atrial fibrillation, cardiac failure

Metastasis- cervical lymph node, boney metastasis, skull . spine, ends of long bones. Lungs.

SPECIAL INVESTIGATION.

THYROID PROFILE- T3, T4, TSH.

ECG

WAYNE'S INDEX

SYMPTOMS

DYSPNOEA ON EFFORT	+1
PALPITATION	+2
TIREDNESS	+2
PREFERENCE FOR HEAT	-5
PREFERENCE TO COLD	+5
EXCESSIVE SWEATING	+3
NERVOUSNESS	+2

APETITE INCREASED +3

APETITE DECREASED -3

WEIGHT INCREASED -3

WEIGHT DECREASED -3

SIGNS	PRESENT	ABSENT
PALPABLE THYROID	+3	-3
BRUIT OVER THYROID	+2	-2
EXOPTHALMOS	+2	
LID RETRACTION	+2	
LID LAG	+1	
HYPERKINESIS	+4	-2
HANDS HOT	+2	-2
HANDS MOIST	+1	-1
CASUAL PULSE RATE		
>80/min		-3
>90/min	+3	
ATRIAL FIBRILATION	+4	

FINAL SCORE

THYROID STATE	SCORE	BIOCHEM VALUE	CORRESPONDS
EUTHYROID	<11	EUTHYROID	YES/NO
HYPERTHYROID	>19	HYPERTHYROID	YES/NO

OBSERVATION AND RESULTS

TOTAL NUMBER OF CASES CORRESPONS CORRECTLY

TOTAL CASE STUDIED- 53

BIOCHEMICAL HYPERTHYROID – 23

WAYNE HYPERTHYROID(>19) - 20(TRUE POSITIVE)

WAYNE DISAMBUIGOUS(11-19) WHO ARE HYPERTHYROID-2(FALSE NEGATIVE)

WAYNE EUTHYROID WHO ARE HYPERTHYROID-1(FALSE NEGATIVE)

BIOCHEMICAL EUTHYROID- 30

WAYNE EUTHYROID-27(TRUE NEGATIVE)

WAYNE DISAMBIGOUS EUTHYROID- 2(TRUE NEGATIVE)

WAYNE HYPERTHYROID WHO ARE EUTHYROID- 1 (FALSE POSITIVE)

CONSOLIDATION

WAYNE TRUE POSITIVE- 20

WAYNE FALSE POSITIVE - 1

WAYNES FALSE NEGATIVE- 3

TRUE NEGATIVE 29

Statistics:-

(a)true positive 20	(b)false positive 1
(C)false negative 3	(d)true negative 29

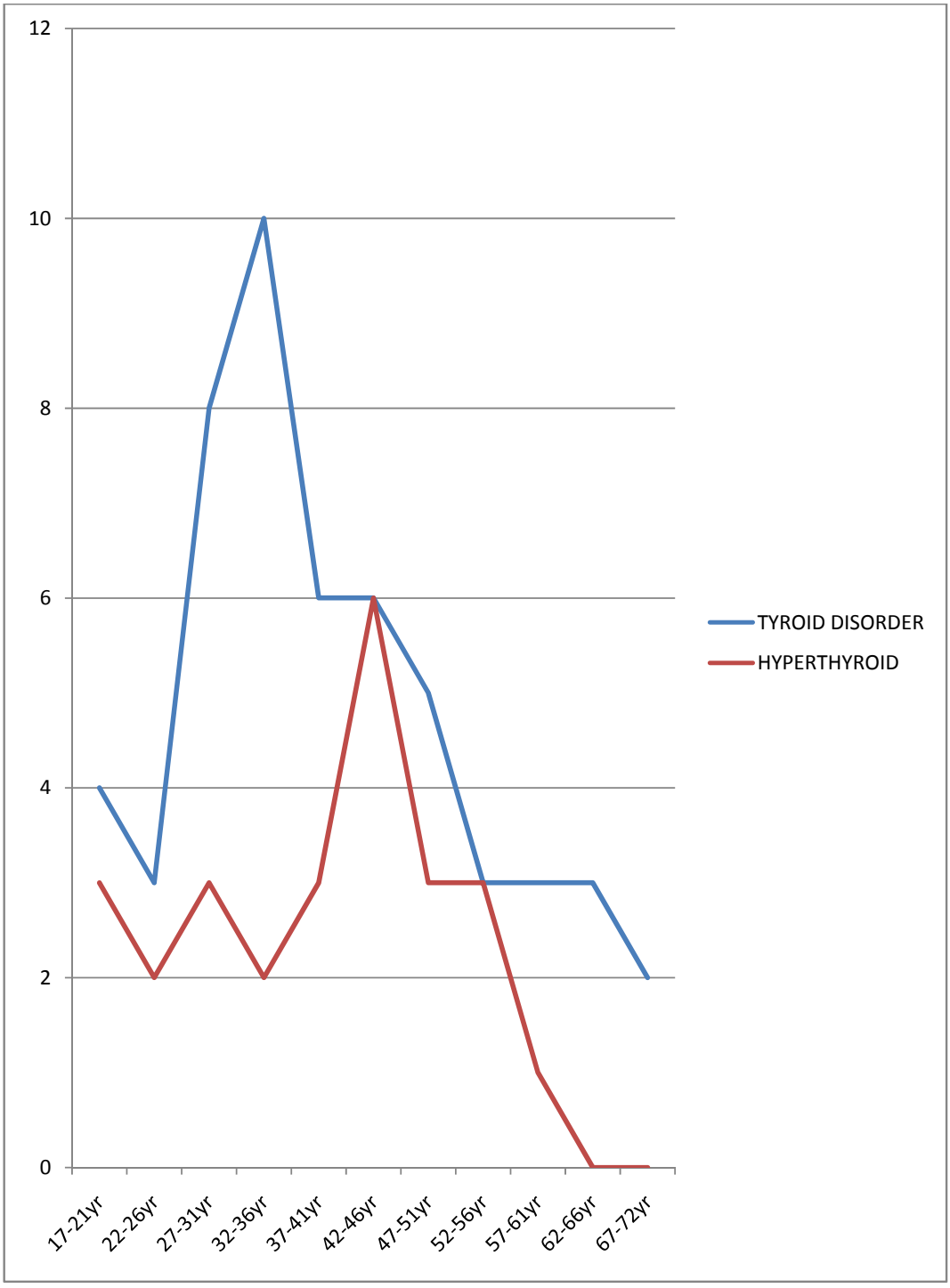
Sensitivity= a/a+c= 20/20+3= 86.9%

Specificity= d/d+b=29/29+1= 96%

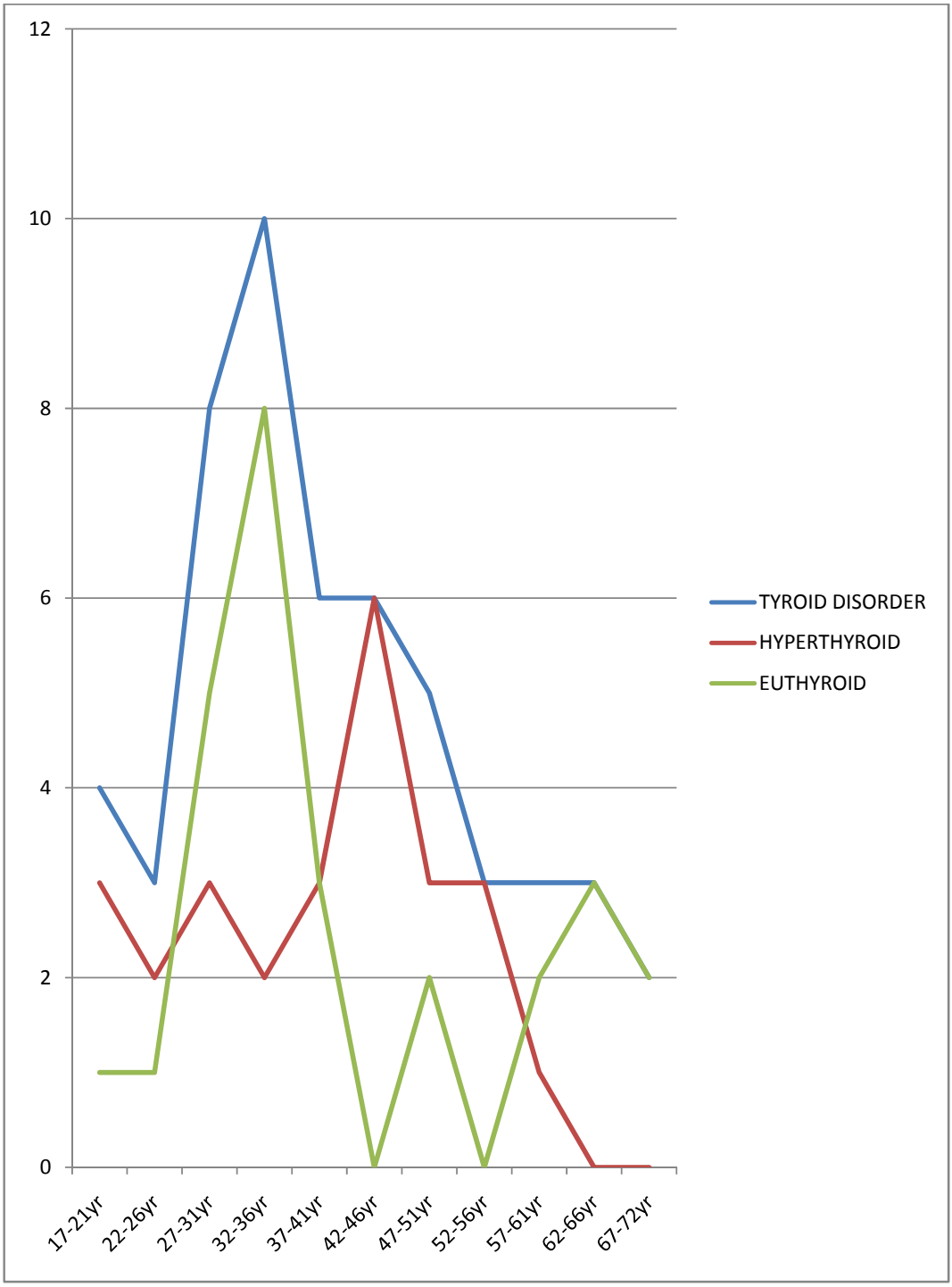
Positive predictive value=a/a+b= 20/23=95.2%

Negative predictive value=d/c+d= 29/3+29=90%

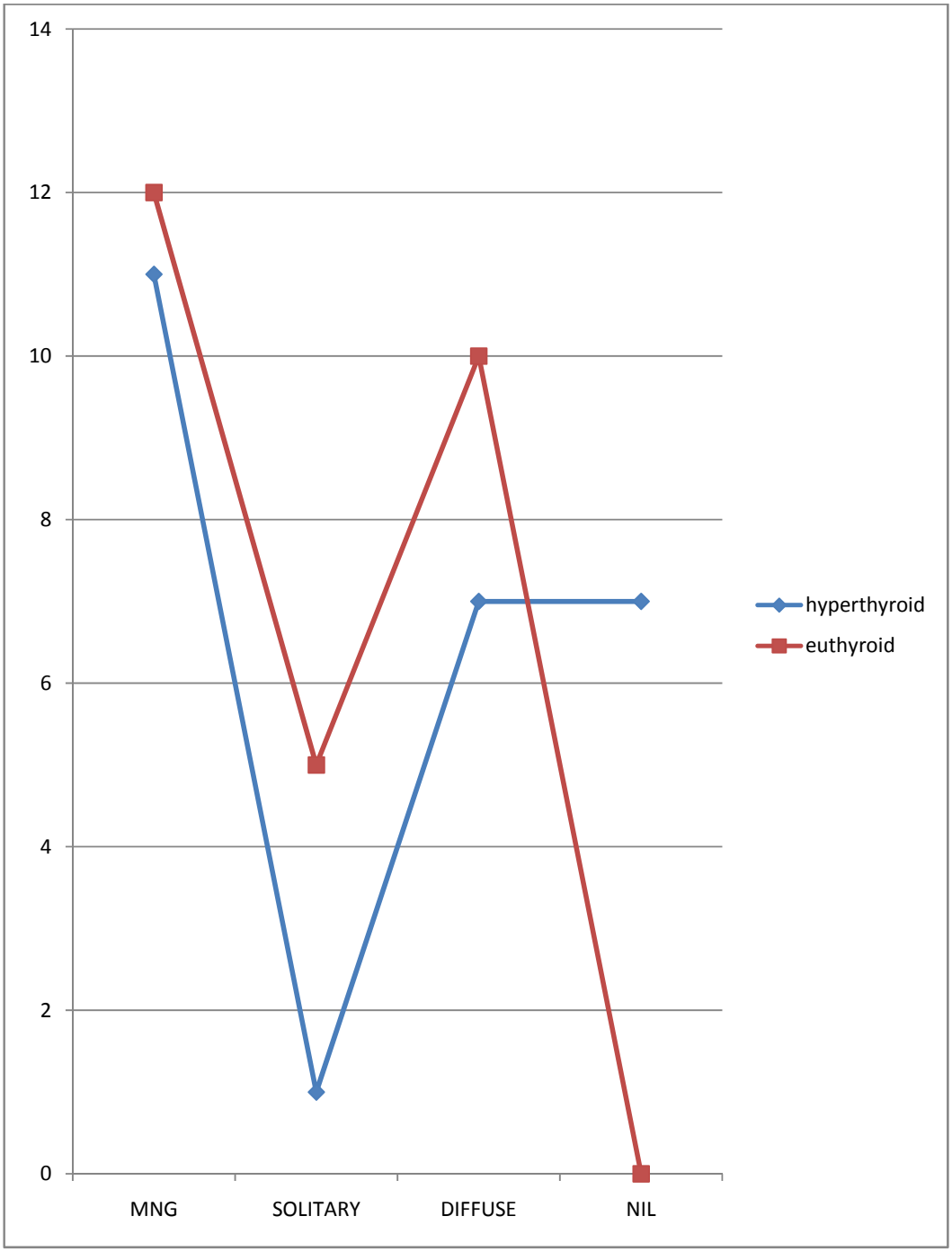
1.Relative frequency of hyperthyroid according to age.



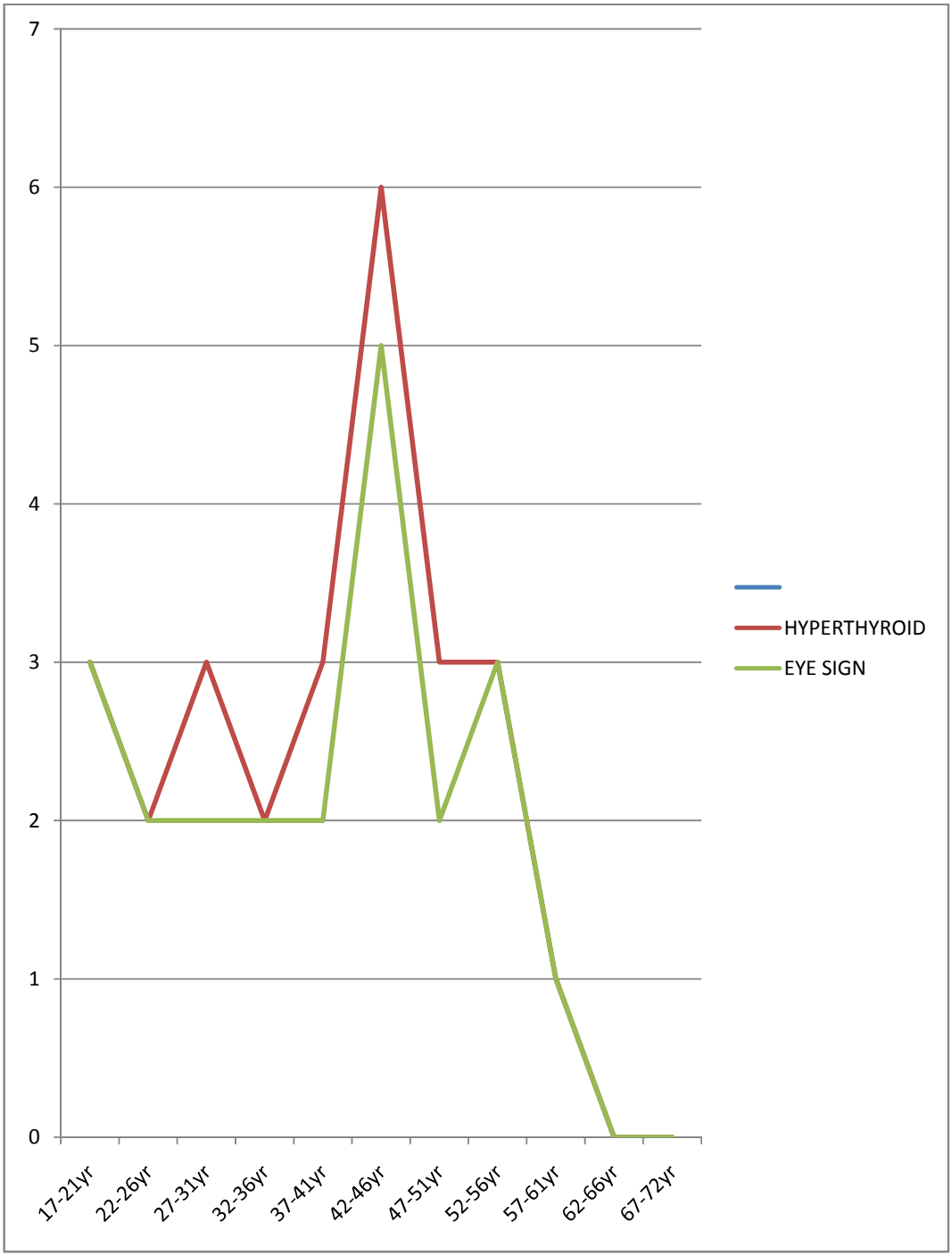
2.Relative frequency of hyperthyroid with euthyroid according to age.



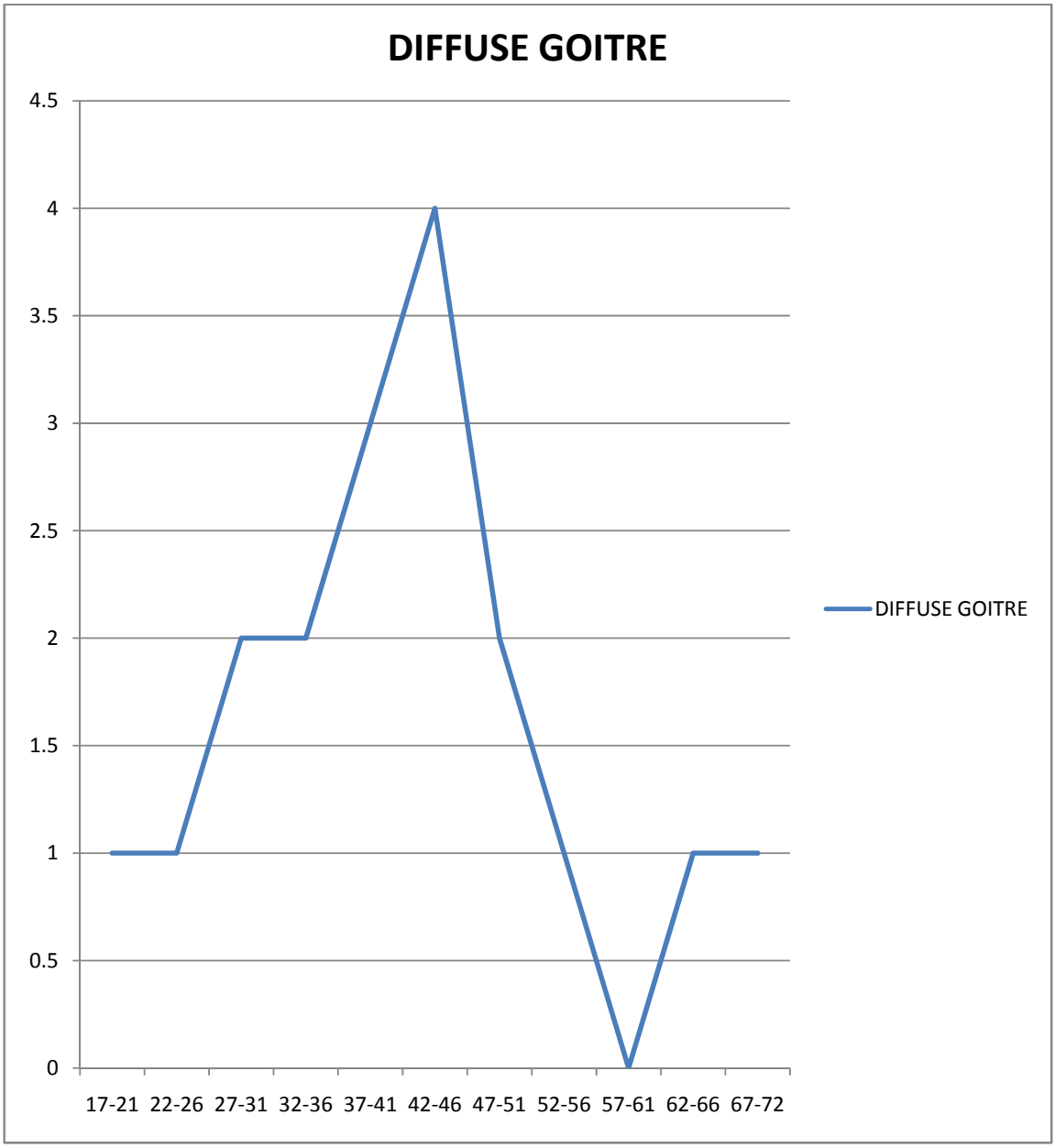
3Clinical relevance of thyroid disorders i.e. frequency of MNG, Solitary Nodule, Diffuse goitre. A composit study.



4.Frequency of eye sign accordance to hyperthyroid with age distribution.



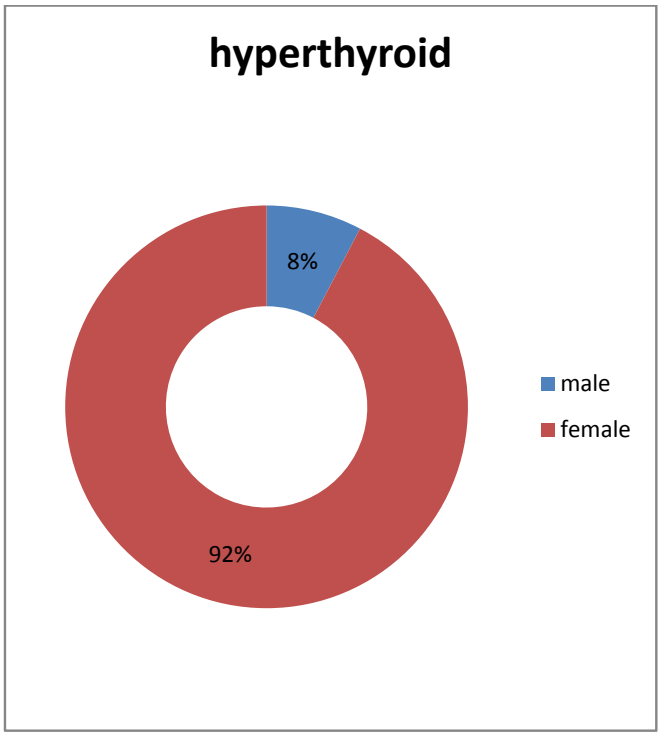
5.Frequency of prevalence of diffuse goitre in different age group.



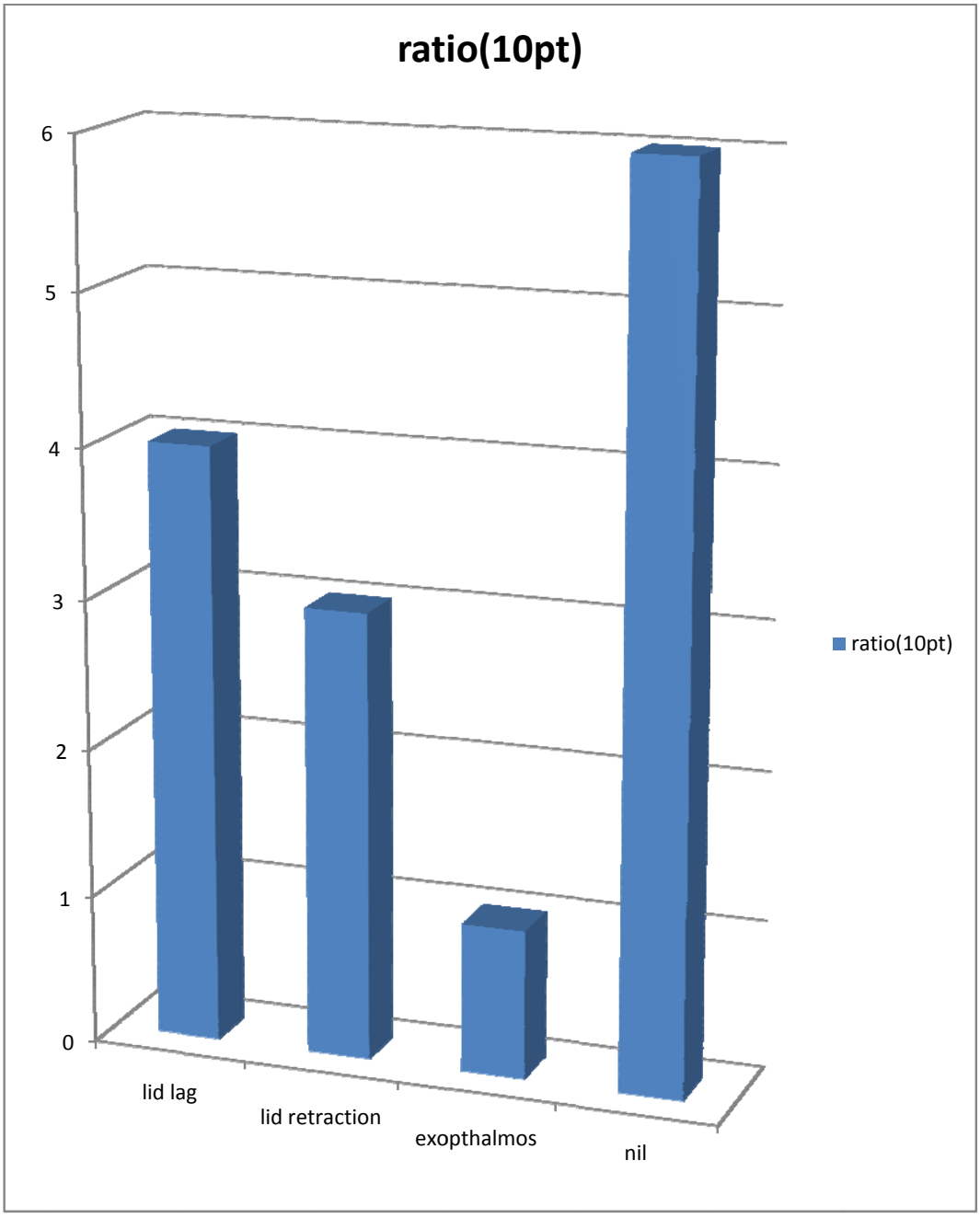
6.Sex wise ratio of hyperthyroidism in our study. We got

Gender	Hyperthyroid
Male	2
Female	24

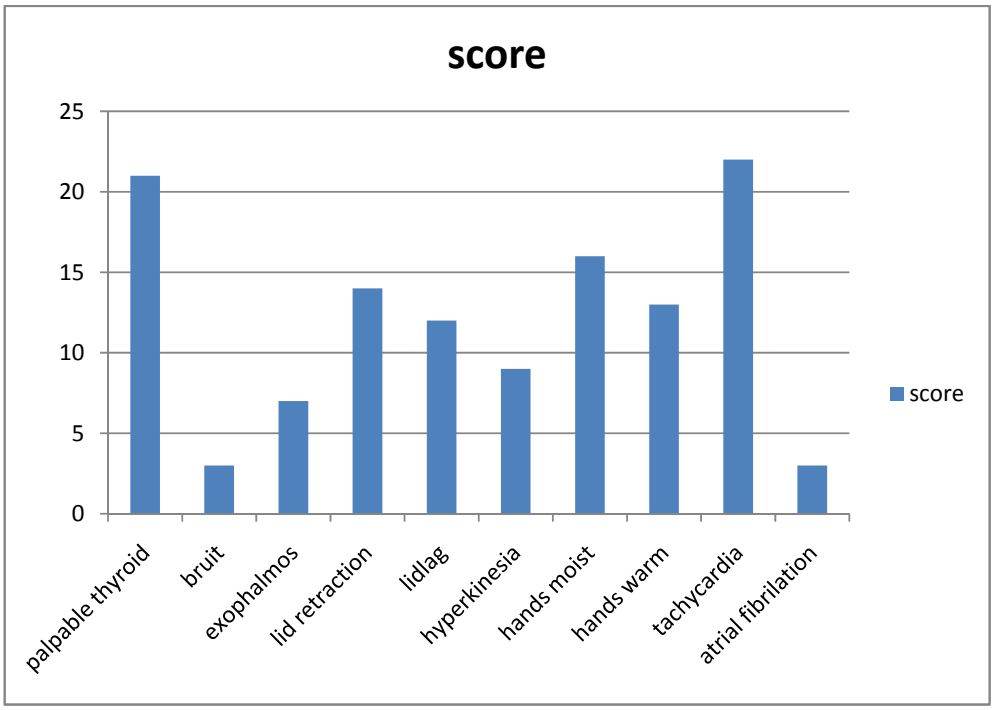
Ratio female:male = 12:1



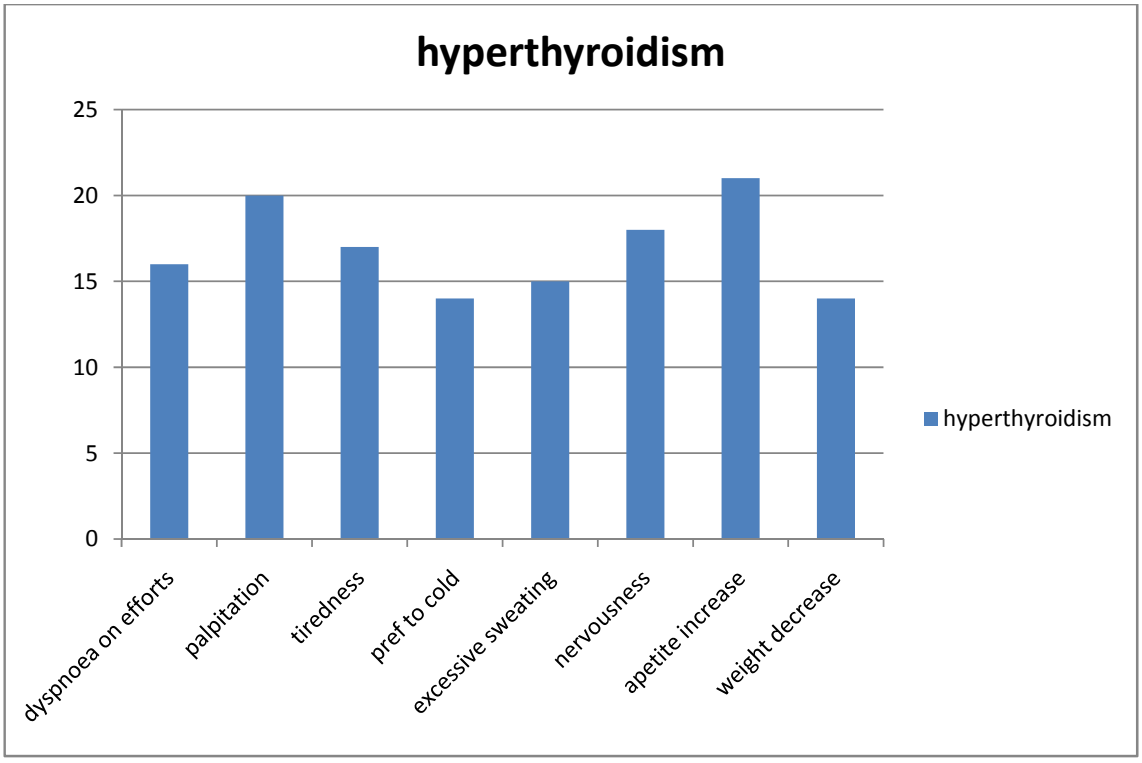
7.Ratio of eye signs in secondary hyperthyroidism.



8.Frequency of occurrence of signs in patients in accordance our study.



9.Frequency of occurrence of symptoms in accordance of our study.



DISCUSSION

- Among our study of 53 patients who presented with symptoms of thyroid dysfunction, we applied wayne's diagnostic criteria to diagnose hyperthyroidism. all patients were biochemically ascertained of their thyroid status and wayne's criteria was assessed for its accuracy by various parameters like specificity.sensitivity, positive predictive value,negative predictive value,

- Sensitivity of 86.9%, specificity 96.6% and negative predictive value 90.2% positive predictive value of 95.2% proves that waynes index stands with near accurate diagnosis which can serve as a costeffective primary modality for diagnosis of hyperthyroidism at basic level.

- There are virtually no studies regarding wayne's criteria in recent literature as it modern diagnostic modalities for hyperthyroidism has taken over.
- Due to patient selection process, by in hospital only, with most selected cases was with appreciable findings and with considerably small number of subjects, our study has significant amount of statistical "BIAS", which is being reflected as such a high results. So by neglecting the concept of bias, for the aspect of statistics , a few charts are made

- Whickham survey by Tunbridge WMG et al, states the prevalence of diffuse goitre decreases with age but greatest in pre-menopausal age group. As per our study results ,the frequency is highest among premenopausal age group, which clearly correlates with our study. But the decreasing order of frequency of prevalence of diffuse goitre is not coinciding. The most possible explanation we can offer is selection bias. Because most of the patients we have selected from surgical wards and op, which automatically excludes paediatrics and adolescent age group.
- According to National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab 2002, by 1. Hollowell JG et al, the ratio of hyperthyroid in male : female is 1:10, and accordind to our study, we got study as male : female as 1:12.
- According to international journal of endocrinology, secondary hyperthyroidism does not present with sever eyes signs except for lid retraction and lid lag, which correlates with our study.
- According to multiple international study, occurrence of hyperthyroidism is highest among reproductive age group females, which is fairly depicted in our study.
- In spite of all advanced diagnostic modalities ,clinical examination should be the first and foremost thing to be stressed as indicated in wayne's criteria, especially in a developing country where extremes of medical care exist.

- Most common sign in our study is palpable thyroid and tachycardia followed by hand moist and hand warm. And the least common presentation are bruit and atrial fibrillation.
- The most common symptom being appetite increase and nervousness, followed by appetite increase and tiredness. The other symptoms which has not been included in waynes criteria are diarrhoea, menstrual irregularities, pruritus , infertility, etc. which is present in many patient.

CONCLUSION

- Waynes criteria holds a good deal of diagnostic accuracy. So it is worth applying this criteria at PHC level, to diagnose and for early referral at higher centre, especially in women of reproductive age group detrimental effects of thyroid disorders on reproduction can be prevented.
- Due to high sensitivity, speficificity,positive predictive value and negative predictive value, wayne's criteria proves basic clinical methods still holds good despite advanced diagnostic modalities
- Inter observer variation is an important limiting factor for waynes criteria, therefore, as score can vary with the observer
- Certain signs and symptoms are not included in wayne's criteria which are not uncommonly encountered in hyperthyroid patients.
- Early diagnosis in paediatric age group is of outmost importance as it can drastically change the outcome as role of thyroid hormones in development and maturation of all organ systems is well known.

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APPENDIX

PROFORMA

Name

Age

Sex

Address

IP/OP number

Date of admission/ Visit

Date of discharge

H/ O Swelling at the base of neck.

H/O Pain

H/O Pressure Effect – Dysphagia, Hoarsness of voice, Dysphonea, Stridor.

Symptoms- loss of weight, preference to cold, excessive sweating, nervous, irritability, insomnia, tremor of hand, weakness of muscle, palpitation, dyspnoea on exertion, exopthalmus, staring gaze. Diplopia, chemosis, amenorrhoea.

Symptoms of secondary thyrotoxicosis.- palpitation, chest pain, signs of cardiac failure

Past history-

Personal history- of dilatory habit and menstruation, bladder and bowel habit.

General survey-

Built and Nourishment-

Facies-

Mental status-

Skin- hot and moist palms

LOCAL EXAMINATION.

THYROID SWELLING WILL BE AT THE BASE OF NECK, MOVES WITH DEGLUTATION, DOES NOT MOVES WITH PROTRUSION OF TONGUE,

PALPATION- Lahey's method, Crile's method, Kocher's test, pemberton sign. . palpation of cervical lymph node.

General Examination-

Primary Toxic manifestations

Eye signs- lid retraction, exopthalmus, Von Graefe's sign, Joffroy's sign, Stellwag sign, Moebius sign, Dalrympte's sign

Opthalmoplegia- weakness of superior and lateral restus

Chemosis of eye.

Tachycardia

Tremors

Moist skin

Thyroid Bruit

Secondary Toxic Manifestations

Cardiovascular system mainly effected, atrial fibrillation, cardiac failure

Metastasis- cervical lymph node, boney metastasis, skull . spine, ends of long bones. Lungs.

SPECIAL INVESTIGATION.

THYROID PROFILE- T3, T4, TSH.

ECG

WAYNE'S INDEX

SYMPTOMS

DYSPNOEA ON EFFORT +1

PALPITATION +2

TIREDNESS +2

PREFERENCE FOR HEAT -5

PREFERENCE TO COLD +5

EXCESSIVE SWEATING +3

NERVOUSNESS +2

APETITE INCREASED +3

APETITE DECREASED -3

WEIGHT INCREASED -3

WEIGHT DECREASED -3

SIGNS	PRESENT	ABSENT
PALPABLE THYROID	+3	-3
BRUIT OVER THYROID	+2	-2
EXOPTHALMOS	+2	
LID RETRACTION	+2	
LID LAG	+1	
HYPERKINESIS	+4	-2
HANDS HOT	+2	-2
HANDS MOIST	+1	-1
CASUAL PULSE RATE		
>80/min		-3
>90/min	+3	
ATRIAL FIBRILATION	+4	

FINAL SCORE

MASTER CHART

IDENTIFICATION/ WAYNES CRITERIA	KUTTIKASI 17/F 23973	RAMYA 17/F 48641	ESAKIAMMAL 20/F 57172	KALA 21/F 30304	RISHI 22/F 56690	BIULA 23/F 14787
DYSPNOEA ON EFFORT(+1/0)	0	0	+1	0	0	0
PALPITATION(+2/0)	+2	0	+2	0	+2	+2
TIREDNESS(+2/0)	+2	+2	+2	0	+2	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0	0
PREFERENCE TO COLD(+5)	+5	0	+5	+5	+5	0
EXCESSIVE SWEATING(+3/0)	+3	0	+3	+3	+3	0
NERVOUSNESS(+2/0)	+2	+2	+2	+2	+2	+2
APETITE INCREASED(+3)	+3	0	+3	+3	+3	+3
APETITE DECREASED(-3)	0	0	0	0	0	0
WEIGHT INCREASED(-3)	0	0	0	0	0	0
WEIGHT DECREASED(+3)	+3	+3	+3	+3	+3	+3
PALPABLE THYROID(+3/-3)	-3	+3	-3	0	+3	-3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2	-2	-2
EXOPTHALMOS(+2/0)	0	0	0	+2	+2	+2
LID RETRACTION(+2/0)	0	0	+2	0	0	0
LID LAG(+1/0)	+1	0	+1	+1	+1	+1
HYPERKINESIS(+4/-2)	0	-2	-2	+4	-2	-2
HANDS HOT(+2/-2)	+2	+2	+2	-2	+2	+2
HANDS MOIST(+1/-1)	+1	-1	+1	+1	+1	+1
PULSE RATE >80(0/-3)	-3	-3	-3	0	-3	-3
PULSE RATE >90(+3)	0	0	0	+3	0	0
ATRIAL FIBRILATION(+4/0)	0	0	0	0	0	0
WAYNE SCORE	20	4	19	25	22	19
T3(0.5-2.0ng/ml)	3.4	1.1	3.2	3.9	4.3	4.5
T4(44-116m.mol/L)	178	89	209	199	197	186
TSH(0.5-7.0mIU/L)	0.032	3.9	0.03	0.029	0.03	0.04
BIOCHEMICALLY	HYPERTHYROID	EUTHYROID	HYPERTHYROID	HYPERTHYROID	HYPERTHYROID	HYPERTHYROID
CLINICAL IMP	MULTINODULAR	SOLITARY	NIL	diffuse	DIFFUSE	MULTINODULAR
CORRESPONDS(Y/N)	Y	Y	Y	Y	Y	N

IDENTIFICATION/ WAYNES CRITERIA	BIKUSI 25/F 34707	MARIAMMAL 27/F 31529	LALITHA 28/F 28507	BHAVANI 28/F 47501	NAMBITHAI 29/F 56894
DYSPNOEA ON EFFORT(+1/0)	0	+1	0	0	0
PALPITATION(+2/0)	0	+2	0	+2	+2
TIREDNESS(+2/0)	0	+2	0	+2	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0
PREFERENCE TO COLD (+5)	0	+5	0	0	+5
EXCESSIVE SWEATING(+3/0)	0	0	0	0	0
NERVOUSNESS(+2/0)	+2	+2	0	0	+2
APETITE INCREASED (+3)	0	+3	0	0	0
APETITE DECREASED (-3)	0	0	0	0	0
WEIGHT INCREASED(-3)	0	0	0	0	0
WEIGHT DECREASED(+3)	0	+3	0	0	0
PALPABLE THYROID(+3/-3)	+3	+3	+3	+3	+3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2	-2
EXOPTHALMOS(+2)	0	0	0	0	+2
LID RETRACTION(+2)	0	0	0	0	0
LID LAG(+1)	0	+1	0	0	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2	-2
HANDS HOT(+2/-2)	-2	-2	-2	-2	-2
HANDS MOIST(+1/-1)	-1	+1	+1	-1	+1
PULSE RATE >80(0/-3)	-3	0	0	-3	0
PULSE RATE >90(+3)	0	+3	0	0	0
ATRIAL FIBRILATION(+4/0)	0	0	0	0	0
WAYNE SCORE	-5	20	-2	-3	13
T3(0.5-2.0ng/ml)	1.3	3.2	1.3	1.2	1.8
T4(44-116m.mol/L)	93	201	67	98	76
TSH(0.5-7.0mIU/L)	5.3	0.02	4.3	4.5	3.2
BIOCHEMICALLY	EUTHYROID	HYPERTHYROID	EUTHYROID	EUTHYROID	EUTHYROID
CLINICAL	DIFFUSE	MNG	MNG	MNG	MNG
CORRESPONDS(Y/N)	Y	Y	Y	Y	N

IDENTIFICATION/ WAYNES CRITERIA	ARUMUGAKANI 29/F 26551	CHERMAKANI 29/F 26013	KAVITHA 31/F 29718	KANITHA 31/F 23405	ALIFATIMA 34/F 26553
DYSPNOEA ON EFFORT(+1/0)	0	0	0	+1	+1
PALPITATION(+2/0)	0	0	+2	+2	+2
TIREDNESS(+2/0)	0	0	0	+2	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0
PREFERENCE TO COLD(+5)	0	0	0	0	+5
EXCESSIVE SWEATING(+3/0)	0	0	+3	0	+3
NERVOUSNESS(+2/0)	0	0	+2	0	+2
APETITE INCREASED(+3)	0	0	+3	+3	+3
APETITE DECREASED(-3)	0	0	0	0	0
WEIGHT INCREASED(-3)	0	0	0	0	0
WEIGHT DECREASED(+3)	0	0	+3	+3	+3
PALPABLE THYROID(+3/-3)	+3	+3	+3	+3	-3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	+2	-2
EXOPTHALMOS(+2/0)	0	0	0	+2	+2
LID RETRACTION(+2/0)	0	0	0	0	0
LID LAG(+1)	0	0	+1	+1	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2	-2
HANDS HOT(+2/-2)	-2	-2	+2	-2	+2
HANDS MOIST(+1/-1)	-1	-1	-1	+1	+1
PULSE RATE >80(0/-3)	-3	0	0	0	0
PULSE RATE >90(+3)	0	0	0	+3	+3
ATRIAL FIBRILATION(+4/0)	0	0	0	+4	0
WAYNE SCORE	-7	-4	14	23	23
T3(0.5-2.0ng/ml)	1.6	1.5	3.9	2.3	1.8
T4(44-116m.mol/L)	75	87	239	203	250
TSH(0.5-7.0mIU/L)	5.5	6.4	0.03	0.02	0.02
BIOCHEMICALLY	EUTHYROID	EUTHYROID	HYPERTHYROID	HYPERTHYROID	HYPERTHYROID
CLINICAL	SOLITARY	DIFFUSE	MNG	SOLITARY	NIL
CORRESPONDS(Y/N)	Y	Y	N	Y	Y

IDENTIFICATION/ WAYNES CRITERIA	GURUAMMAL 34/F 39036	ALAGUMUTTU 34/F 36914	MUKUAMMAL 35/F 23377	AIYAMMAL 36/F 29816
DYSPNOEA ON EFFORT(+1/0)	+1	0	0	0
PALPITATION(+2/0)	+2	+2	0	0
TIREDNESS(+2/0)	+2	0	0	0
PREFERENCE FOR HEAT (-5)	0	0	0	0
PREFERENCE TO COLD(+5)	0	0	0	0
EXCESSIVE SWEATING(+3/0)	0	0	0	0
NERVOUSNESS(+2/0)	0	+2	0	0
APETITE INCREASED(+3)	0	0	0	0
APETITE DECREASED(-3)	0	0	0	0
WEIGHT INCREASED(-3)	0	0	0	0
WEIGHT DECREASED(+3)	0	0	0	0
PALPABLE THYROID(+3/-3)	+3	+3	+3	-3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2
EXOPTHALMOS(+2/0)	0	0	0	0
LID RETRACTION(+2)	0	0	0	0
LID LAG(+1)	0	0	0	0
HYPERKINESIS(+4/-2)	-2	-2	-2	-2
HANDS HOT(+2/-2)	-2	-2	-2	-2
HANDS MOIST(+1/-1)	-1	-1	-1	-1
PULSE RATE >80(0/-3)	-3	-3	-3	-3
PULSE RATE >90(+3)	0	0	0	0
ATRIAL FIBRILATION(+4/0)	0	0	0	0
WAYNE SCORE	-2	-3	-7	-13
T3(0.5-2.0ng/ml)	0.9	1.3	1.1	1.6
T4(44-116m.mol/L)	87	95	83	106
TSH(0.5-7.0mIU/L)	4.6	5.3	5.2	6.3
BIOCHEMICALLY	EUTHYROID	EUTHYROID	EUTHYROID	EUTHYROID
CLINICAL	MNG	MNG	DIFFUSE	MNG
CORRESPONDS(Y/N)	Y	Y	Y	Y

IDENTIFICATION/ WAYNES CRITERIA	KALIAMMAL 36/F 39066	MUSAIK 36/F 24041	PASUPATI 36/F 29801	MUTHULAKSMI 37/F 34457	VALIAMAL 38/F 36106
DYSPNOEA ON EFFORT(+1/0)	0	+1	+1	0	0
PALPITATION(+2/0)	0	+2	+2	0	0
TIREDNESS(+2/0)	0	+2	+2	0	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0
PREFERENCE TO COLD(+5)	0	+5	+5	0	0
EXCESSIVE SWEATING(+3/0)	0	+3	+3	0	+3
NERVOUSNESS(+2/0)	0	+2	+2	-	+2
APETITE INCREASED(+3)	0	+3	+3	-	+3
APETITE DECREASED(-3)	0	0	-3	-	0
WEIGHT INCREASED(-3)	0	0	0	0	0
WEIGHT DECREASED(+3)	0	-3	+3	0	+3
PALPABLE THYROID(+3/-3)	-3	-3	+3	+3	+3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2	-2
EXOPTHALMOS(+2/0)	0	+2	+2	0	0
LID RETRACTION(+2/0)	0	+2	+2	0	0
LID LAG(+1/0)	0	+1	+1	0	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2	-2
HANDS HOT(+2/-2)	-2	+2	+2	-2	+2
HANDS MOIST(+1/-1)	-1	+1	+1	-1	+1
PULSE RATE >80(0/-3)	-3	-3	-3	-3	0
PULSE RATE >90(+3)	0	0	0	0	+3
ATRIAL FIBRILATION(+4/0)	0	0	0	0	0
WAYNE SCORE	-13	16	22	-7	19
T3(0.5-2.0ng/ml)	1.5	4.9	3.9	1.8	3.6
T4(44-116m.mol/L)	95	270	185	76	203
TSH(0.5-7.0mIU/L)	6.5	0.1	0.04	5.0	0.02
BIOCHEMICALLY	EUTHYROID	HYPERTHYROID	HYPERTHYROID	EUTHYROID	HYPERTHYROID
CLINICAL	SOLITARY	NIL	DIFFUSE	DIFFUSE	MNG
CORRESPONDS(Y/N)	Y	N	Y	Y	Y

IDENTIFICATION/ WAYNES CRITERIA	MUTHUSELVI 32/F 14243	GOMATHI 38/F 60608	MUTHUSELVI 38/F 14243	PETCHIAMMAL 42/F 43365	VASANTA 42/F 49862
DYSPNOEA ON EFFORT(+1/0)	0	0	+1	+1	0
PALPITATION(+2/0)	+2	+2	+2	+2	+2
TIREDNESS(+2/0)	0	0	+2	+2	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0
PREFERENCE TO COLD(+5)	+5	0	+5	0	0
EXCESSIVE SWEATING(+3/0)	+3	0	+3	0	+3
NERVOUSNESS(+2/0)	+2	0	+2	0	+2
APETITE INCREASED (+3)	+3	0	0	0	+3
APETITE DECREASED(-3)	0	0	0	0	0
WEIGHT INCREASED(-3)	0	0	-3	0	0
WEIGHT DECREASED(+3)	+3	0	0	0	+3
PALPABLE THYROID(+3/-3)	+3	+3	+3	+3	+3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2	-2
EXOPTHALMOS(+2/0)	+2	0	+2	0	+2
LID RETRACTION(+2/0)	+2	0	0	0	0
LID LAG(+1)	+1	0	+1	0	+1
HYPERKINESIS(+4/-2)	+4	-4	-2	-2	-2
HANDS HOT(+2/-2)	+2	-2	+2	-2	+2
HANDS MOIST(+1/-1)	+1	-1	+1	-1	+1
PULSE RATE >80(0/-3)	0	-3		-3	0
PULSE RATE >90(+3)	+3	0	+3	0	+3
ATRIAL FIBRILATION(+4/0)	0	0	0	0	0
WAYNE SCORE	38	-7	20	-2	23
T3(0.5-2.0ng/ml)	3.2	1.2	3.4	1.0	4.2
T4(44-116m.mol/L)	208	65	223	77	234
TSH(0.5-7.0mIU/L)	0.1	3.4	0.1	4.2	0.02
BIOCHEMICALLY	HYPERTHYROID	EUTHYROID	HYPERTHYROID	EUTHYROID	HYPERTHYROID
CLINICAL	MNG	SOLITARY	DIFFUSE	MNG	MNG
CORRESPONDS(Y/N)	Y	Y	Y	Y	Y

IDENTIFICATION/ WAYNES CRITERIA	RAYAMMAL 43/F 30663	SUSIYAMMAL 43/F 25286	RUKMANI 43/F 10371	KALIAMMAL 45/F 39630	ESAKIAML 48/F 50655
DYSPNOEA ON EFFORT(+1/0)	0	0	0	0	0
PALPITATION(+2/0)	+2	+2	+2	+2	0
TIREDNESS(+2/0)	0	+2	+2	0	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0
PREFERENCE TO COLD(+5)	0	0	0	+5	+5
EXCESSIVE SWEATING(+3/0)	0	0	0	+3	+3
NERVOUSNESS(+2/0)	+2	0	+2	+2	+2
APETITE INCREASED(+3)	0	0	+3	+3	0
APETITE DECREASED(-3)	0	0	0	0	0
WEIGHT INCREASED(-3)	0	-3	+3	0	0
WEIGHT DECREASED(+3)	0	0	+3	+3	0
PALPABLE THYROID(+3/-3)	+3	-3	+3	+3	-3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2	-2
EXOPTHALMOS(+2/0)	+2	0	+2	+2	0
LID RETRACTION(+2/0)	0	0	+2	0	0
LID LAG(+1/0)	+1	0	+1	+1	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2	-2
HANDS HOT(+2/-2)	+2	-2	+2	+2	-2
HANDS MOIST(+1/-1)	+1	-1	+1	+1	+1
PULSE RATE >80(0/-3)	-3	-3	-3	0	0
PULSE RATE >90(+3)	0	0	0	+3	+3
ATRIAL FIBRILATION(+4/0)	0	0	0	0	0
WAYNE SCORE	6	-10	19	25	8
T3(0.5-2.0ng/ml)	3.4	1.3	3.2	2.3	3.2
T4(44-116m.mol/L)	302	102	199	302	189
TSH(0.5-7.0mIU/L)	0.04	5.2	0.02	0.03	0.03
BIOCHEMICALLY	HYPERTHYROID	EUTHYROID	HYPERTHYROID	HYPERTHYROID	HYPERTHYROID
CLINICAL IMP	DIFFUSE	DIFFUSE	MNG	MNG	NIL
CORRESPONDS(Y/N)	N	Y	Y	Y	N

IDENTIFICATION/ WAYNES CRITERIA	MUTHULAKSHMI 45/F 45676	SELVUM 49/M 877 9	CHELLADURAI 49/M 12163	PAPATHI 50/M 60791	RAJAMML 50/F 19471
DYSPNOEA ON EFFORT(+1/0)	+1	+1	0	0	0
PALPITATION(+2/0)	+2	+2	+2	0	+2
TIREDNESS(+2/0)	+2	+2	+2	0	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0
PREFERENCE TO COLD(+5)	+5	+5	0	0	+5
EXCESSIVE SWEATING(+3/0)	+3	+3	+3	0	+3
NERVOUSNESS(+2/0)	+2	+2	+2	0	0
APETITE INCREASED(+3)	+3	+3	+3	0	+3
APETITE DECREASED(-3)	0	0	0	0	0
WEIGHT INCREASED(-3)	0	0	0	-3	0
WEIGHT DECREASED(+3)	0	+3	+3	0	+3
PALPABLE THYROID(+3/-3)	+3	-3	+3	-3	-3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2	-2
EXOPTHALMOS(+2/0)	+2	+2	+2	0	+2
LID RETRACTION(+2/0)	0	0	+2	0	0
LID LAG(+1/0)	+1	+1	+1	0	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2	-2
HANDS HOT(+2/-2)	+2	-2	+2	-2	+2
HANDS MOIST(+1/-1)	+1	+1	+1	+1	+1
PULSE RATE >80(0/-3)	0	-3	0	-3	0
PULSE RATE >90(+3)	+3	0	+3	0	+3
ATRIAL FIBRILATION(+4/0)	0	0	0	0	0
WAYNE SCORE	26	16	24	-14	20
T3(0.5-2.0ng/ml)	2.3	3.4	2.2	1.3	2.6
T4(44-116m.mol/L)	190	184	232	98	254
TSH(0.5-7.0mIU/L)	0.02	0.032	0.022	4.2	0.10
BIOCHEMICALLY	HYPERTHYROID	HYPERTHYROID	HYPERTHYROID	EUTHYROID	HYPERTHYROID
CLINICAL	MNG	NIL	MNG	MNG	NIL
CORRESPONDS(Y/N)	Y	N	Y	Y	Y

IDENTIFICATION/ WAYNES CRITERIA	MARISHWARI 52/F 5689	ARUMUGAMML 52/F 20089	RAMALAKSHMI 55/F 58040	ANNAKILI 57/F 11250
DYSPNOEA ON EFFORT(+1/0)	0	+1	0	+1
PALPITATION(+2/0)	+2	+2	0	+2
TIREDNESS(+2/0)	+2	0	0	+2
PREFERENCE FOR HEAT (-5)	0	0	0	0
PREFERENCE TO COLD (+5)	+5	0	0	0
EXCESSIVE SWEATING(+3/0)	+3	0	0	+3
NERVOUSNESS(+2/0)	+2	0	0	+2
APETITE INCREASED(+3)	0	0	0	+3
APETITE DECREASED(-3)	0	0	0	0
WEIGHT INCREASED(-3)	0	0	0	0
WEIGHT DECREASED(+3)	0	0	0	+3
PALPABLE THYROID(+3/-3)	+3	-3	+3	+3
BRUIT OVER THYROID(+2/-2)	-2	-2	0	-2
EXOPTHALMOS(+2/0)	+2	0	0	+2
LID RETRACTION(+2/0)	0	0	0	+2
LID LAG(+1/0)	0	0	+1	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2
HANDS HOT(+2/-2)	-2	-2	-2	-2
HANDS MOIST(+1/-1)	+1	-1	+1	+1
PULSE RATE >80(0/-3)	0	-3	-3	0
PULSE RATE >90(+3)	+3	0	0	0
ATRIAL FIBRILATION(+4/0)	0	0	0	0
WAYNE SCORE	17	-10	-2	19
T3(0.5-2.0ng/ml)	2.5	1.2	1.3	1.4
T4(44-116m.mol/L)	201	109	98	96
TSH(0.5-7.0mIU/L)	0.1	4.2	3.2	3.1
BIOCHEMICALLY	HYPERTHYROID	EUTHYROID	EUTHYROID	EUTHYROID
CLINICAL	DIFFUSE	DIFFUSE	MNG	MNG
CORRESPONDS(Y/N)	N	Y	Y	N

IDENTIFICATION/ WAYNES CRITERIA	ANNAMANI 57/F 35787	KANIAMMA 63/F 28465	ROSE PUSPM 65/F 14846	VELAMTHI 67/F 60001	SUBBULAKSHI 65/F 22468
DYSPNOEA ON EFFORT(+1/0)	+1	0	+1	0	+1
PALPITATION(+2/0)	0	0	+2	+2	+2
TIREDNESS(+2/0)	0	0	+2	+2	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0	0
PREFERENCE TO COLD(+5)	0	0	0	0	0
EXCESSIVE SWEATING(+3/0)	0	0	0	0	0
NERVOUSNESS(+2/0)	0	0	+2	0	+2
APETITE INCREASED(+3)	0	0	0	0	0
APETITE DECREASED (-3)	0	0	0	0	0
WEIGHT INCREASED (-3)	0	0	0	0	0
WEIGHT DECREASED(+3)	0	0	+3	0	+3
PALPABLE THYROID(+3/-3)	+3	+3	+3	+3	-3
BRUIT OVER THYROID(+2/-2)	-2	-2	-2	-2	-2
EXOPTHALMOS(+2/0)	0	0	+2	0	+2
LID RETRACTION(+2/0)	0	0	+2	+2	0
LID LAG(+1/0)	0	0	+1	+1	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2	-2
HANDS HOT(+2/-2)	-2	-2	-2	-2	-2
HANDS MOIST(+1/-1)	-1	-1	-1	-1	-1
PULSE RATE >80(0/-3)	-3	-3	0	-3	-3
PULSE RATE >90(+3)	0	0	0	0	0
ATRIAL FIBRILATION(+4/0)	0	0	0	0	0
WAYNE SCORE	-6	-7	11		0
T3(0.5-2.0ng/ml)	1.3	0.9	1.2	1.1	1.2
T4(44-116m.mol/L)	98	87	97	89	78
TSH(0.5-7.0mIU/L)	4.2	3.9	4.1	4.3	4.9
BIOCHEMICALLY	EUTHYROID	EUTHYROID	EUTHYROID	EUTHYROID	EUTHYROID
CLINICAL	DIFFUSE	SOLITARY	MNG	DIFFUSE	DIFFUSE
CORRESPONDS(Y/N)	Y	Y	Y	Y	Y

IDENTIFICATION/ WAYNES CRITERIA	PONMANIAMMAL 68/F 32748	SUNMUGA 40/F 50250	KALADEVI 40/F 33053	RAMALAKSHMI 60/F 40345
DYSPNOEA ON EFFORT(+1/0)	0	0	+1	+1
PALPITATION(+2/0)	0	0	+2	+2
TIREDNESS(+2/0)	+2	0	0	+2
PREFERENCE FOR HEAT(-5)	0	0	0	0
PREFERENCE TO COLD(+5)	0	+5	0	+5
EXCESSIVE SWEATING(+3/0)	+3	+3	0	0
NERVOUSNESS(+2/0)	+2	0	0	+2
APETITE INCREASED(+3)	+3	0	+3	0
APETITE DECREASED(-3)	-3	0	0	0
WEIGHT INCREASED(-3)	0	0	0	0
WEIGHT DECREASED(+3)	+3	+3	+3	+3
PALPABLE THYROID(+3/-3)	+3	-3	+3	+3
BRUIT OVER THYROID(+2/-2)	+2	-2	-2	-2
EXOPTHALMOS(+2/0)	0	0	0	0
LID RETRACTION(+2/0)	+2	0	0	0
LID LAG(+1/0)	+1	0	0	+1
HYPERKINESIS(+4/-2)	-2	-2	-2	-2
HANDS HOT(+2/-2)	+2	-2	-2	-2
HANDS MOIST(+1/-1)	+1	-1	-1	-1
PULSE RATE >80(0/-3)	0	0	-3	0
PULSE RATE >90(+3)	+3	+3	0	0
ATRIAL FIBRILATION(+4/0)	0	0	0	0
WAYNE SCORE	19	4	-2	12
T3(0.5-2.0ng/ml)	3.2	3.2	0.8	1.9
T4(44-116m.mol/L)	226	289	65	98
TSH(0.5-7.0m.IU/L)	0.02	0.1	6.3	5.4
BIOCHEMICALLY	HYPERTHYROID	HYPERTHYROID	EUTHYROID	EUTHYROID
CLINICAL	MNG	NIL	DIFFUSE	MNG
CORRESPONDS(Y/N)	Y	N	Y	N